A Dissertation on

SCREENING FOR OCULAR MANIFESTATIONS OF TUBERCULOSIS AT THE TIME OF DIAGNOSIS OF PULMONARY TUBERCULOSIS.

Submitted to the

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

In partial fulfillment of the Regulations

for the Award of the Degree of

M.S. (BRANCH - III)

OPHTHALMOLOGY

GOVT. STANLEY MEDICAL COLLEGE AND HOSPITAL

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI – 600 001.

APRIL 2016

CERTIFICATE

This is to certify that the study entitled **"SCREENING FOR OCULAR MANIFESTATIONS OF TUBERCULOSIS AT THE TIME OF DIAGNOSIS OF PULMONARY TUBERCULOSIS"** is the result of original work carried out by **DR.M.PRATHEEBA**, under my supervision and guidance at **STANLEY MEDICAL COLLEGE, CHENNAI**. The thesis is submitted by the candidate in partial fulfilment of the requirements for the award of **M.S Degree in ophthalmology**, course from 2013 to 2016 at the Stanley medical college, Chennai.

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DECLARATION

I hereby declare that this dissertation entitled **"Screening for Ocular Manifestations of Tuberculosis at the Time of Diagnosis of Pulmonary Tuberculosis**" is a bonafide and genuine research work carried out by me under the guidance of **Prof.Dr.K.BASKER, M.S.,D.O.,** HOD, Department of ophthalmology, Government Stanley medical college and hospital, Chennai-600001.

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Place:

ACKNOWLEDGEMENT

I express my deep gratitude to Prof. Dr. ISAAC CHRISTIAN MOSES M.D., Dean, stanley medical college, Chennai for permitting me to do this study.

With overwhelming respect and gratitude, I thank Prof. & HOD Dr.K.BASKER M.S.,D.O., for giving this opportunity to work on this thesis project, his valuable advice and guidance, in this endeavour. His kind attitude and encouragement have been a source of inspiration throughout this study, which helped me to do my best in this effort.

I am very grateful to Prof.Dr.RADHAKRISHNAN M.S.,D.O., and Prof.Dr.THANGERANI RAAJASEHARAN M.S.,DO., for their continuous support and guidance.

I am thankful to Prof. Dr.S.SRIDHAR M.D,DTCD., HEAD OF THE DEPARTMENT, CHEST MEDICINE, Chennai for his support and guidance without which this would not have been possible.

I am very grateful to my assistant professors

Dr.T.R.ANURADHA M.S., Dr.S.VENKATESH M.S.,

Dr.P.GEETHA M.S.,D.O., Dr.B.MEENAKSHI M.S.,

Dr.S.HEMAPRIYA,D.O.,DNB., Dr.V.SAVITHRI M.S.,D.O.,

Dr.IMAYA GANESAN, MS., for rendering their valuable suggestions, supervision throughout the progress of work.

I am thankful to all my colleagues and friends for their support.

Finally I am deeply indepted to all my patients for their sincere cooperation for completion of this study.

It is my earnest duty to thank my parents and my family without whom accomplishing this task would have been impossible.

Date:

Place:

INSTITUTIONAL ETHICAL COMMITTEE, STANLEY MEDICAL COLLEGE, CHENNAI-1

Title of the Work : Screening for Ocular manifestations of TB at the time of diagnosis of pulmonary TB. A clinical study.

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Designation : PG in MS (Ophthalmology)

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The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 11.02.2014 at the Council Hall, Stanley Medical College, Chennai-1 at 2PM

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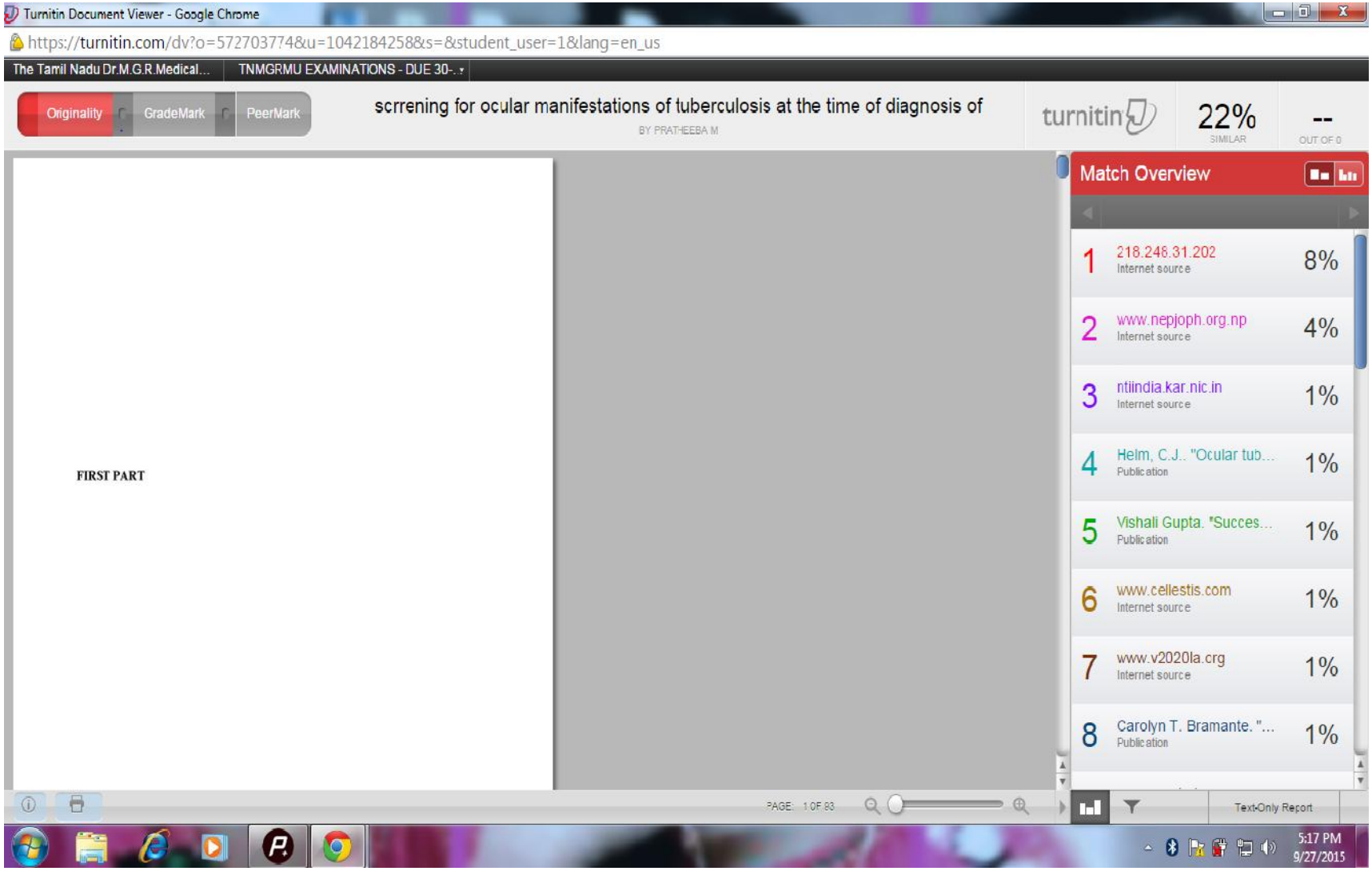
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CONTENTS

PART–I

PART–II

ANNEXURE

PART – I

INTRODUCTION

Tuberculosis is a common infectious disease which is prevalent in our country caused by Mycobacterium tuberculosis, a bacteria or also by other related members comprising the TB complex. In our country Tuberculosis is a major public health problem with high mortality and mobidity. Mycobacterium tuberculosis infection causes a wide range of clinical problems which may be a mere asymptomatic infection or pulmonary tuberculosis or extra pulmonary tuberculosis ultimately may lead to death. Ocular tuberculosis is one of the extra pulmonary type in tuberculosis. In 5% of infected patients, progressive primary disease develops within 1 to 2 years. 90% of primarily infected patients remain asymptomatic and are identified only by conversion from PPD negative to positive .In the rest of 5% of primary infected persons, disease develops several to many years later ("post primary tuberculosis"). Roughly 60% of patients with extra pulmonary tuberculosis have no evidence of pulmonary tuberculosis and when tuberculosis manifests as uveitis, accurate diagnosis becomes increasingly difficult as biopsy samples are not easily available. Thus diagnosis of tubercular uveitis can only be presumed when the patient presents with associated symptoms like chronic evening fever or evidence of other extra pulmonary tuberculosis, any radiological findings or conversion of Mantoux skin test.

REVIEW OF LITERATURE

HISTORY:

It is well known that Mycobacterium tuberculosis evolved in human beings from M.Bovis sometime after the domestication of cattle, that is between 4000 and 800 B.C. earliest description of ocular tuberculosis was credited by Maitre-jan in 1711,iris lesion described by him which lead on to corneal perforation..(3) choroidal tubercles in miliary tuberculosis was first described by gueneau mussy in 1830.(4) anatomical description of the lesion was given by jaeger 1855.(5) choroidal tubercles was first demonstrated by fraenkel with the ophthalmoscope.(6) Tubercles in the choroid of eye known as choroidal tubercles which was seen clinically by cohnheim those were identical with tubercles else where in the body , and on injecting the tuberculous material experimentally produced in guinea-pigs.(7) Von Graefe and Leber in 1868 given the detailed ophthalmoscopic descriptions.. In 1882 Koch discovered the tubercle bacillus, and Von Michel 1883 identified the organism in the eye.(8). Koch's also discovered a fluid medium in which tubercle bacilli could be grown and he designated it as lymph and afterward as tuberculin- a substance he thought might provide a cure for the disease. Later it was thought as a material that contained tuberculoprotein or degradation products of the proteins that were able to elicit hypersensitivity reactions. The tuberculin which had the most widespread 4 use was called Koch's Old tuberculin. It was prepared by taking a liquid medium in which tubercle bacilli

had been grown, sterilizing it with heat, producing a bacteria free filtrate, and then concentrating it by evaporation to one- tenth of its original volume.(9) The first tuberculin test material was prepared by Robert Koch. Its use for detection of tuberculin was first described in 1907 by Von Priquet. (9) He demonstrated that when tuberculin was injected intra dermally in tuberculous child, a papule 5-20mm in diameter appeared at the site and then gradually disappeared over a period of 8 days or longer. He also introduced the word "Allergy" to designate this changed or altered state since children who were not infected with tubercle bacilli were found to have a negative response to the allergy test.(10) Tuberculin gradually lost favour as a therapeutic modality and its value to test for allergy to tuberculosis gained recognition. It came to be used in patients with aim of discriminating between various forms of tuberculosis or for use in judging prognosis. This lead to the use of intra dermal injection of tuberculin as introduced by Mantoux in 1910(11), and this method has stood the test of time because the intra dermal injection of 0.1ml of a carefully prepared solution of the test material is the most accurate way to perform the tuberculin test. Today, the Mantoux test is the most widely used

Woods' 4 categories can be summarized as follows:

1. Foreign body-like reaction (e.g., miliary tubercles of the iris and choroid)

2. Acute circumscribed inflammation that may recur if the patient's resistance decreases (e.g., sclerokeratitis, Eales disease)

3. Chronic inflammation with multiple recurrence (e.g., ciliary body tuberculoma)

4. Acute, rapidly spreading inflammation with necrosis, caseation, and occasionally a ruptured globe (tuberculous panophthalmitis)

BASIC MECHANISMS OF INFECTION:

The eye can become infected with TB through several different mechanisms.

1. The most common form of ocular involvement is from hematogenous spread. The uveal tract (composed of the iris, ciliary body, and choroid) is the coat of the eye most frequently involved, presumably because of its high vascular content.

2. Primary exogenous infection of the eye, can occur in the lids or in the conjunctiva. Other external tissues more rarely infected include the cornea, sclera, and lacrimal sac.

3. Secondary infection of the eye may occur by direct extension from surrounding tissues or by contamination with the patient's own sputum.

4. Additionally, some forms of ocular TB, such as phlyctenular disease and Eales disease, are thought to be the result of a hypersensitivity reaction.

5. Rich's law states that the extent of a tuberculous lesion is propotinate directly to virulence and number of tuberculous bacilli and also nature of hypersensitivity of that infected tissue.

Pathophysiology :

The causative organism of tuberculosis is M. tuberculosis. It is an obligate, non-motile, aerobic, non-spore forming, slow growing bacterium. The only natural host are human beings. The primary mode of spread is airborne route through aerosol which enters the host through the lungs causing latent infection or dormant infection, with immune system functioning normally. Mycobacterium Avium-intracellulare Complex (MAC) in addition to M tuberculosis must be taken into account in case of AIDS patients. Disease following infection is caused immediately after exposure within first few years in case of 5% of patients. Reactivation of latent infection is seen in 5% of patients who develop the disease after several years of exposure due to alteration in host immunity

When the patient's immune system fails, symptoms occur which is influenced by many factors such as age, immunosuppressant drugs and disease. The bacteria leaves no tissue or organ in the body as it can invade everything. For infection to occur in the humans 5-200 inhaled bacilli is enough. In case of immune compromised individuals the disease may progress rapidly. It also invades the lymphatic system i.e., lymph nodes and to extrapulmonary sites through hematogenous spread.

The end organs that are commonly affected such as lung apex, bones, kidneys, eye , choroid, meninges have a high regional oxygen-tension. Among all the ocular structures the choroid and ciliary body have a high oxygen tension where the organism grows well. The bacterium infects the reticuloendothelial system with preference to macrophages though infects the other cells too..

In case of dissemination of tuberculosis genetic susceptibility of the patients may play a role. Protection and control of tuberculosis infection is related to Th1 cell response. Development of active disease is seen in patients where Th2 responses predominate, not able to contain the disease. Ocular tuberculosis is seen in 1% to 2% of tuberculosis patients which usually masquerades like other infectious & disease processes. Caseating granulomatous lesion and necrosis are the characteristic features of extrapulmonary tuberculosis. Extrapulmonary tuberculosis can occur separately in isolation without pulmonary involvement or may be associated with pulmonary TB.

2. EPIDEMIOLOGY

Tuberculosis remains the primary killer of adults in developing countries despite the existence of cost effective tools that can cure the disease.

SYSTEMIC TUBERCULOSIS GLOBALLY

Globally 8.8 million persons developed tuberculosis (all forms) in the year 2005 of which 3.9 million people were sputum positive cases, and caused 1.5 million deaths. According to 2005 statistics global tuberculosis incidence of all forms, sputum positive was 136/lakh population and 60/lakh population respectively. Prevalence of tuberculosis was 217/lakh population and mortality due to TB was 24/lakh population.South east Asian Region carries excessive number of world burden of tuberculosis that is 34% which is disproportionate with worlds buden of 25% . (12) IN INDIA In India in the year 2008 , Incidence of all cases, sputum positive cases was 168 and 75per one lakh population .Prevalence of all forms was 283/one lakh population. Mortality was 28/ lakh population13Every day in India more than 20,000 people become infected with the tubercle bacillus, more than 5000 develop the disease, and more than 1000 die from TB14.

OCULAR EPIDEMIOLOGY:

Ocular TB prevalence rates are not known exactly because of lack of standard data. The rarity (1.4%) of ocular tuberculosis has been emphasized in the past in sanatorium patients admitted for active tuberculosis.(15,16) However, in a recent prospective study of 300 culture-proven patients with tuberculosis ,the authors randomly selected 100 patients from the series to document ophthalmic changes;(18) selected showed lesions suggestive of ocular tuberculosis and they mainly consisted of choroiditis besides papillitis,

retinitis, vasculitis, dacryoadenitis and scleritis.(17)Tubercular etiology of uveitis has been a controversial issue ever since reports from Wilmer institute indicated the decline of tuberculosis as an etiology of granulomatous uveitis from 80% in 1941 to 20% in 1960, indicating a lack of rigid diagnostic criteria in the earlier reports.(18) More recent data from the United States described tubercular etiology in less than 0.5% patients managed in a tertiary care uveitis service.(19) However, in Japanese population increasing frequency of tubercular etiology has been reported at 6.9% ahead of Behcets disease (5.8%) among 189 referred patients with uveitis.(20) A retrospective study done in Riyadh (Saudi Arabia), Islam and Tabbara (2002) in which 200 uveitis patients were analysed which showed only 10.5% of uveitis with tubercular etiology second to herpetic uveitis (16%).(21) In India, where tuberculosis is endemic, of the 602 patients who obtained a specific diagnosis among 1233 in patients of uveitis who attended uveitis clinic in a tertiary care centre in North India, about 30% had infective etiology ,and tuberculosis accounted for 70% of these and was far commoner than toxoplasmosis (11.7%).(22)Previously however, a report from south India found tubercular etiology only in 0.39% of the 1273 patients.(23)

BACTERIOLOGY:

Tuberculosis is caused by tubercle bacilli of mycobacteriaceae family. Human beings are the reservoir and are highly susceptible to Tuberculosis. Tubercle bacilli are aerobic, non motile, non-capsulated, non-sporing, straight

or slightly curved rods about 3 micrometers x 0.3 micrometer, occurring singly, in pairs or as small clumps. Tubercle bacilli are difficult to stain, but once stained with carbolfuschin or florochromeauramine, they resist decolourisation with dilute acids and alcohol hence they are known as acid fast bacilli (AFB).On culture media, M. tuberculosis colonies are rough, dry, raised, hard texture and creamy white in colour and appear only after a minimum of 2 weeks of incubation.(24) Colonies of human tubercle bacilli generally appear on egg (Lowenstein Jensen) media after 2-3 weeks at 35 degree Celsius. Increased CO2 tension enhances growth. The growth rate is much slower than most of other bacteria. The 8 doubling time of tubercle bacilli is about 18hr.(25) The niacin test is useful to differentiate M. tuberculosis bacilli from other species in same family.

PATHOGENESIS

PATHOGENESIS OF SYSTEMIC TUBERCULOSIS:

Tuberculosis is a droplet infection which carries particles each particle has one to three bacilli, they are all able to reach the lung alveoli and can set up the infection. Tubercle bacilli do not contain or secrete a toxin. The bacillus is ingested and either destroyed by the resident alveolar macrophage (AM), or it may thrive causing necrosis of the phagocyte. Recruitment of circulating neutrophils, lymphocytes and monocytes occurs because of the generation of Cytokines and chemokines during the process. Lymphokines that are generated during the process of tuberculous antigen presentation,and the

monocytes which transform into epitheliod giant cells that can stop the spread of local infection .Above this reaction results in formation of granuloma which contains central area of necrosis that contains acid fast bacilli. (26-29) in the beginning stage of infection, The bacilli contained cells of monocytes and histocytes will gain the access to lymphatic channels and blood circulation via entered into many organs they will remain dormant in that area, Those contained epitheloid cells and T cells which are resistant to host. occurance of active pulmonary tuberculosis is mainly due to the presence of dormant mycobacteria in the pulmonary and extra pulmonary sites in case of adults.

PATHOGENESIS OF TUBERCULAR UVEITIS:

In the form of extra pulmonary TB of other area of the body, ocular manifestations of tuberculosis also results from the hematogenous seeding from pulmonary area or else from the reactivation of the dormant lesion in the ocular tissue, one is more important for the presentation of ocular lesions. Reactivation is a process in which it needs the presence of virulent bacteria and the number of bacilli, resistance of the host in the form of available number of sensitized TH1 cells (30) The latter could be the most common cause for the active ocular lesions and the clinical manifestations. The reactivation or the seeding may depend on number and virulence of bacilli, host resistance in the form of availability of sensitized TH1 helper cells and their activation state, nutritional status, and age of the individual.(31) Histopathogenesis of the iris in tubercular anterior uveitis reveals evidence of

lymphocytes, histiocytes, and plasma cells, and may display necrotizing granuloma. The mutton fat keratic precipitates are a collection of lymphocytes and macrophages. The ciliary body is seen with caseating granuloma characterized by central necrosis surrounded by epitheloid and giant cells. Acid fast stain shows bacilli in epitheloid cells. Cases of tubercular anterior uveitis are due to secondary manifestation of the disease with extra pulmonary involvement and reactivation of the M. tuberculosis in ocular tissue. The disease is brought under control by the interaction between macrophages and the T lymphocytes. Delayed Type IV hypersensitivity reactions are the cause of formation of tuberculomata in the iris with localized central necrosis surrounded by macrophages with proliferating bacilli numerous cytokines are involved in the control of proliferation of mycobacterial bacilli including tumour necrosis factor alpha (TNF-alpha) .Cell- 10 mediated immunity is involved in the control of the mycobacterial infectious process. Both CD4+ (helper) T-lymphocytes and CD8+ (suppressor) T lymphocytes are involved in keeping the bacilli at bay. Subsequently healing may result in calcification. The tuberculin skin test becomes positive after 6 to 8 weeks as the cell-mediated immunity develops.(32)

TABLE-1

FACTORS AFFECTING THE HOST DEFENCE MECHANISM AGAINST TUBERCULOSIS

Malnutrition
Toxins • Tobacco • Alcohol
Corticosteroids
Immunosuppressants
Other diseases • HIV infection • Diabetes • Leprosy • Silicosis • Leukemia • Measles • Whooping cough
Low socio-economic status
Race

TABLE-2

AGE RELATED MANIFESTATIONS OF TUBERCULOSIS(24)

Age	Presentation
Age under one year	Miliary tuberculosis, Tuberculous meningitis
Age 1 to puberty	primary lung lesion, chronic disseminated tuberculosis, miliary tuberculosis, tubercular meningitis
Adolescent/Young adult	Pulmonary tuberculosis
Middle aged Males Females	Pulmonary tuberculosis
Old age Males Females	Pulmonary tuberculosis

CLINICAL FEATURES

SYSTEMIC PRESENTATIONS (24)

CONSTITUTIONAL SYMPTOMS

The most common symptom of a patient with tuberculosis is Fever which is usually of low grade at the onset of the disease. It may change to high grade with the disease progression. Evening rise of temperature is often noticed. The other symptoms are night sweats, tiredness, fatigue, weight loss and anorexia.

PRIMARY PULMONARY TUBERCULOSIS

Infection with Mycobacterium tuberculosis in the first time causes primary pulmonary tuberculosis. Highly endemic areas tuberculosis presents as primary pulmonary tuberculosis which will be common in most of children and adolescents. In children majority of the time the primary pulmonary tuberculosis is asymptomatic, without any evidence in chest radiography. Tuberculin skin test helps in its diagnosis which earlier tested negative turns positive. The alveolar macrophages engulf the bacilli which multiplies leading on to pneumonia of tuberculousetiology forming a subpleural focus located in the lower part of upper part (Ghon focus) or lower lobe. It may also cause enlargement of hilar lymph nodes. The term PRIMARY COMPLEX refers to the above said Ghon focus along with hilar lymph node enlargement. It takes about 3 to 8 weeks for it to develop after infection along with tuberculin hypersensitivity. The primary infection in most of the case heals spontaneously and in few calcification develops. Even after healing few bacilli may remain latent surviving in the healed lesion. In some patients whose immunity is impaired or associated with other risk factors, commonly in children, the primary lesion may enlarge and invade other structures leading onto meningeal, miliary or other disseminated forms of the disease. Fever and cough sometimes associated pleuritic chest pain are the commonest findings in primary pulmonary tuberculosis of children.

POST PRIMARY PULMONARY TUBERCULOSIS

These type of the disease more commonly seen with adults in endemic area. The latent infection may get reactivated (post primary progression) which is endogenous reactivation or may be due to endogenous reinfection differing from the primary type in various aspects. This type of tuberculosis mostly seen in adults. The chest radiography of these patients typically shows upper lobar infiltrates which may be unilateral or bilateral that progresses from necrosis, tissue destruction ultimately lads to cavity formation. Unusual involvement may be that of lymph node. The tissue or material that goes in for necrosis breaks into the airways, causing expectoration with sputum fully laden with bacteria. The sputum is the source of infection through which it spreads to the contacts. In case of immune deficient patients the disease progresses to wide spread dissemination both in lungs or in other end organs. Cough typically lasts for three weeks or more which may be dry or productive. The sputum that is produced may be either mucoid or purulent. The diagnosis of pulmonary tuberculosis is made by demonstrating the acid fast bacilli in the sputum. The patients may get breathlessness due to the progression of disease or due to complications like pleural effusion, pneumo thorax or bronchial asthma

ABDOMINAL TUBERCULOSIS

In case of patients with sub-acute, acute or chronic illness peritoneal tuberculosis may occur. The clinical features may be weight loss, diarrhoea, pallor and distended abdomen with ascites. The abdominal pain may be localised to right lower quadrant with tenderness that may be elicited in the right iliac fossa. In case of intestinal perforation signs of acute peritonitis can be elicited.

NEUROLOGICAL TUBERCULOSIS

Tubercular meningitis occurring in childhood is the recent trend. In the period of -6 weeks the clinical involvement of the disease will occur. The clinical features of initial stage are vague ill health, anorexia, apathy & behavioural changes. As the disease progresses to meningitis the symptoms are fever, vomiting and headache. Preceding the signs of meningeal irritation and associated features of raised intra cranial tension and focal neurological deficit . Major complications are cranial nerve palsies and visual loss which may be complete or incomplete. The end stage will be characterised by deep coma with decorticate or decerebrate posture. With in 5-8 weeks death occurs if there is no treatment.

SKELETAL TUBERCULOSIS

Skeletal tuberculosis includes involvement of knee joint, hip or spine and also may present as osteomyelitis and tubercular tenosynovitis. The

presenting complaints will be pain over the affected site which complicates the movements of joints. During sleep, muscle relaxation will occur it causes painful movements lead on to night cries. Localized knuckle kyphosis involving the dorsal spine along with vertebral wedging or collapse are the signs of spinal tuberculosis. Large gibbus may lead on to deformities in the thoracic cage. Cold abscesses developed in the regions of neck,chest wall,inguinal region,groin,thigh.Tuberculosis involvement of hip joint if not treated it will lead on to 3 stages of pathological process, on coming to the first stage that is synovitis in which hip attained the position of flexion, abduction and external rotation. in the next stage is late arthritis . In tuberculosis of knee joint recurrent attacks of synovitis occurs which increases in severity and persistent. Hamstrings initially develop spasm, later atrophy and contracture occurs with triple deformity in advanced stage which is characteristic of TB. Tenosynovitis of tubercular etiology commonly occurs in hand with signs and symptoms of pain, weakness of grip, limitation of movements and tenderness. Skin, eye, otorhinolaryngology, lymph node, female genitourinary tract are the other organs that are involved in tuberculosis.

OCULAR TUBERCULOSIS

PRIMARY vs SECONDARY OCULAR TUBERCULOSIS

Ocular involvement of tuberculosis is of two types namely primary and secondary. In Primary ocular tuberculosis the initial portal of entry into the body is through the eyes whereas in case of secondary ocular tuberculosis it

occurs due to the spread of infection from adjacent structure or through hematogenous spread from lungs. The entry of tubercle bacilli into the eye through intact conjunctival or corneal epithelium penetrating it was investigated. It was demonstrated by Finnoff in experimental animals, he states that break in the epithelium important for the infection occur due to concentrated bacilli laden sputum or topical emulsion. Primary ocular tuberculosis can occur only when there is a prior injury to the epithelium thereby gaining access. Lymph node caseation was found to be present only at the initial infection site by the investigators. Further caseation of other lymph nodes is considered to be prevented by the development of delayed hypersensitivity. Therefore lymph node caseation is not considered as a differentiating feature between primary and secondary ocular infection. In case of primary ocular infection, it is confined to the conjunctiva and cornea whereas involvement of intra-ocular structures and orbit are almost always a result of secondary infection that occurs due to spread from systemic disease.

OCULAR TUBERCULOSIS MANIFESTATIONS

ADNEXA

Adnexial involvement are listed as, from the eye lids

Lupus vulgaris,scrofuloderma,tubercular tarsitis

ANTERIOR SEGMENT

Anterior segment involvement is listed as,

Phlyctenulosis, conjunctival granuloma, diffuse scleritis, sclerokeratitis, nodular scleritis, iris nodules, uveitis, chronic anterior segment uveitis, angle nodules, cyclitis, interstitial keratitis, cataract, secondary glaucoma, papillary block glaucoma

POSTERIOR SEGMENT

Posterior segment involvement as ,sub retinal abscess, multifocal choroidal tubercles, solitary choroidal tuberculoma, endophthalmitis, serpiginous like choroiditis, retinal vasculitis, neuroretinitis

The organism can invade any of the structures of eye or adnexa. It will be a chronic and insidious disease when it involves the anterior segment.

EYELIDS

The progressive infection of the skin in eyelids by TB is called as Lupus vulgaris. The clinical course will be a slowly progressive one. The characteristic feature will be sub-epithelial nodule with an apple jelly appearance. The lesions that are produced by Tuberculous tarsitis can simulate the chalazion.

LACRIMAL SYSTEM

The infection of the lacrimal gland is the Tuberculousdacroadenitis and the infection of the lacrimal sac is termed as Tuberculous dacryocystitis. Pathologically the lesion of the lacrimal gland may be a sclerotic one or a caseous type. The signs of the disease will be a firm non-tender enlargement involving the lacrimal gland with proptosis and restriction of ocular movements with ptosis.

CONJUNCTIVA

The mode of infection in case of Primary conjunctival tuberculosis is either by self-inoculation of the mucous membrane by the organism from contaminated handkerchief with sputum or through the airborne droplet infection. It is commonly seen in the children. In case of Secondary conjunctival tuberculosis, it develops from the spread of infection from lesions of adjacent skin such as lupus vulgaris or vesicular rash of TB etiology. Conjunctival tuberculosis was classified into four types by Eyre which was later modified by Duke-Elder. The following are the types of conjunctival involvement namely polypoidal conjunctivitis, hypertrophic conjunctivitis, nodular conjunctivitis, ulcerative conjunctivitis. It is with identification of Acid Fast Bacilli either by culture or biopsy, the diagnosis of conjunctival tuberculosis is made. Phlyctenulosis is commonly seen in children with malnutrition. It is characterized by a nodule, the involvement is due to localized hypersensitivity to the antigens of mycobacterium tuberculosis, the

commonest site being limbus but can also occur in the conjunctiva. The symptoms will be irritation, photophobia, blepharospasm and tearing. The gross appearance of the nodules will be pinkish-grey in colour and the center will be soft, localized, elevated with a leash of blood .

PHLYCTEN

DISEASE OF SCLERA

Infection of the sclera occurs secondary to either by local spread from foci within the eye or due to hematogenous spread of infection. Anterior part is more commonly involved whereas posterior sclera involvement is very rare in tuberculosis. The disease process is of two types namely localized or diffuse involvement. Localized anterior scleritis is more common than diffuse variety which is characterized by an area of focal elevated nodules that are dark red in colour with chronic granulomatous inflammation characteristic of TB along with caseous necrosis. The complication may be scleromalacia and if left

untreated on time may result in scleral perforation. Incase of diffuse scleritis, it is characterised by inflammation involving the peripheral stroma in a triangular fashion along with scleritis causing Sclerokeratitis.

CORNEA

Phlyctenularkeratoconjunctivitis is caused by tuberculosis infection, staphylococcal blepharitis or parasite infection with Tb etiology being the most common cause. It is caused by non-specific allergic response to a foreign protein in the cornea and conjunctiva.Corneal involvement lead on to interstitial keratitis and stromal infiltration. It can occur alone or may coexist with uveitis incase of more extensive involvement and scleritis. The symptoms will be redness of eyes, tearing and foreign body sensation with severity based on extent of corneal involvement. They appear as a small nodule in the periphery limbus region which later migrates to the center with superficial vessels dragging along with it. The epithelium of the involved part of cornea will be previously intact which on progression is eroded forming a defect in the epithelium.

UVEAL TUBERCULOSIS

The presentation of Uveal tuberculosis may be of two types namely Chronic anterior uveitis and Disseminated choroiditis. The symptoms may be unilateral or bilateral in patients with anterior uveitis which are photoohobia, redness and few may see floaters. Incase of bilateral involvement the symptoms may be asymmetric with inflammatory signs varying in each eye.

Mutton fat keratic precipitates are the characteristic feature of anterior uveitis which may be few in number or diffuse involvement of the corneal endothelium. It may cause corneal edema in those patients. The keratic precipitates may vary in size from moderate to large, white-yellow in colour. Incase of long standing uveitis, pigment granules maybe present in mutton fat kps cells. Cells and flare may be present in the anterior chamber and localized nodules may be present in the angles of anterior chamber which may cause anterior synechiae. Microscopic examination of patients with iris tuberculosis revealed lesions that are identical to military tubercular lesion found in other parts of the body. The types of Iris nodules are named as koeppe's and bussaca's nodules may or may not be present in a case of iris TB. The nodules may vary in size from small to large with thickened iris that may lose its anterior surface normal architecture. Episodes of exacerbation may be seen in ocular tuberculosis patients with active anterior uveitis, the anterior chamber showing severe exudates. The kps may be modified in patients on topical steroids whose size may become small with non-granulomatous appearance. In chronic uveitis, posterior synechiae may be formed where there will be formation of adhesions posteriorly to the anterior surface of lens capsule causing Iris bombe and iris diaphragm may be displaced anteriorly causing pupillary block glaucoma. Cataract changes may be seen in the lens signs of vitritis may be seen in anterior vitreous due to ciliary body involvement.

CHOROIDAL TUBERCLES

In tubercular posterior uveitis the most characteristic presentation clinically are the multifocal choroidal tubercles which proves that the mode of spread of tubercular bacilli from lungs or other sites is through hematogenous route causing intra-ocular tuberculosis. The tubercles of choroid are usually multiple in number and the diameter is less than 5 in number it can be unilateral or bilateral. The tubercles are greyish white to yellow in colour, present deep in the choroids and are discrete with indistinct border. They occur mostly in the posterior pole measuring a quarter disc to several discs in diameter. There may be serous detachment over which the tubercles may lie. Healing of choroid tubercles occur over a period of 12 to 14 weeks leaving a pale atrophic areas with sharp demarcation and variable pigmentation. Tubercles may be detected in routine examination in patients with Aquired Immuno-Deficiency Syndrome(AIDS) which may be asymptomatic without any apparent clinical signs of inflammation such as haemorrhage, exudation or serous detachment.

SOLITARY CHOROIDAL TUBERCULOMA/SUBRETINAL ABSCESS

Tuberculoma may occur as a solitary raised mass like lesion in Ocular tuberculosis. Size of the lesion may vary from 4 to 14 mm. be present as solitary elevated mass like lesion (tuberculoma) measuring 4 to14mm in size. Due to progression of the disease there will be liquefied caseous necrosis and tissue destruction with rapid multiplication of the tubercular bacilli resulting in

the lesion. When the lesion is large there will be a yellowish subretinal mass along with exudative retinal detachment. When the disease progresses rapidly it breaks into the vitreous cavity or even result in perforation.

ENDOPHTHALMITIS

Occurrence of acute onset endogenous endophthalmitis in ocular tuberculosis is very rare and it happens when the disease is rapidly progressive not responding to antitubercular drugs.Endophthalmitis may occur when the multiplication of Koch's bacilli is rapid or in the setting of patients receiving corticosteroids therapy without antitubercular therapy concomitantly.

TUBERCULAR SERPIGINOUS LIKE CHOROIDITIS

Multifocal progressive choroiditis is a manifestation of ocular tuberculosis which may start as a discrete and non-contiguous lesion which later progresses relentlessly with a progressive edge that resembles serpiginous choroiditis. The morphological patterns observed are two in number as follows: 1) Progressive multifocal choroiditis– here the lesions start as discrete ones which later progresses like a wave turning confluent. The lesions are yellowish-white in colour with well-defined round edges and the size of the lesions range from one-fourth to 1disc diameter with raised margins. 2) Plaque-like lesion that may begin to appear more diffusely with edges being serpiginous with active progression. Initially the lesions are large in size during the time of presentation, plaque-like yellowish white lesions with

elevated edges occurring diffusely. The centre of the lesion will be elevated with pigmentary changes which shows the process of healing in the centre.

TUBERCULAR NEURORETINITIS

Retrobulbar optic neuritis complicating tubercular meningitis will be the presentation of Tubercular optic neuropathy. Exudative retinal detachment that occurs in tubercular multifocal choroiditis may rarely be preceded by neuroretinitis. The signs may be optic disc edema and macular star that may complicate the tubercular retinal vasculitis.

TUBERCULAR RETINAL VASCULITIS

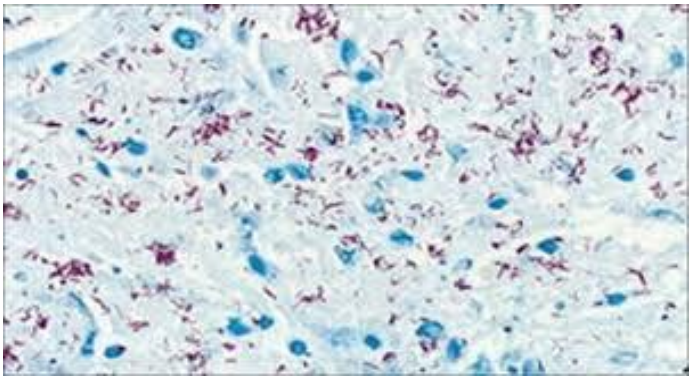
The cause for vasculitis in ocular tuberculosis is still debatable. The two possibilities are either vasculitis is caused due to the presence of tubercular bacilli or just a hypersensitivity reaction to the tubercular antigen causing vasculitis. Vasculitis caused due to Mycobacterium tuberculosis can be proved by a vitreous or aqueous humour tap in which M.tuberculosis DNA can be detected by PCR (polymerase chain reaction). It can also be detected in patients with retinal vasculitis from the surgically removed epiretinal membranes. In active vasculitis, patients may present with moderate vitritis and severe perivascular cuffing with infiltrates. Due to extensive capillary non-perfusion in the periphery new vessels are formed both in the periphery and also on the optic disc. Inferiorly in the vitreous cavity snowball opacities can be identified. Active or healed choroiditis patches below the retinal vessels are present in almost half of the patients with tubercular retinal vasculitis.

Macular star and optic disc edema that are characteristic of neuroretinitis are commonly seen with tubercular retinal vasculitis. The neo-vascularization seen in the periphery of the retina due to extensive peripheral ischemia are treated with scatter LASER photocoagulation in majority of the cases. Pars plana vitrectomy is another procedure that is commonly done to remove the vitreous haemorrhage that is non-clearing or to relieve from the tractional detachment.

TESTS FOR DIAGNOSIS OF TUBERCULOSIS:

DIAGNOSTIC TESTS FOR TUBERCULOSIS:

ZIEHL-NEELSEN TECHNIQUE



Conformation of ocular tuberculosis need the identification of mycobacterium tuberculosis in ocular tissue or fluids. The procedure is unfortunately very difficult and obtaining the tissue also very difficult in eye, eventhough obtaining the sample in that identification of mycobacterium tuberculosis is also difficult. Prior to enucleation the diagnosis is rarely confirmed. The obtained material should be divided for both microscopic and culture examination. Examination under the microscopy is easiest procedure

and we can rapidly identify the presence of acid fast bacilli. Sputum microscopic examination is the one to specifically establish the diagnosis of pulmonary tuberculosis ,the method is most reliable, sensitive, specific and inexpensive, and established widely 38. In HIV patients, children, and extra-pulmonary disease is difficult to maintain the capacity and expertise for reliable microscopic examination of sputum, requires repeated patients visit and it is insensitive 39.extremely low concentration of mycobacteria obtained from the samples of aqueous and vitreous. positive results are obtained by using the technique of centrifugation. Ziehl-Neelsen, acid fast stain or a fluorescent acid-fast stain used to stain the smear both of them with equal sensitivity69.Formalin is used to fixate the smear for histologic examination .collection of modified macrophages or epitheloid cells surrounded by a rim of lymphocytes indicates granulomatous inflammation. clusters of epitheloid cells and langerhans type cells seen with the muli nucleated giant cells. Caseation may be present or not some other causes for granulomatous infections are leprosy,syphilis,cat scratch disease,brucellosis,and various fungal infections. multiple sections should be examined, because single section will not yield the mycobacterium tubercle bacilli, it is very difficult to find in both the eyes and elsewhere. Highest yield of mycobacterium bacilli obtained from caseating granulomas. 2.aqueous and vitreous fluid specimens inoculated into the liquid medium immediately such as middlebrook 7H-9,Lowenstein-jensen,dubos tween albumin broth, or proskauer-beck broth, at a ratio not greater than part fluid specimen to 5 to 10 parts of liquid medium.

unlike sputum, ocular tissue should be expected to be free of contamination. sterile containers should be used for specimen collection, no preservatives or fixatives should be used. Sterile tissue grinder is used to homogenized the specimen ,small amount of sterile 0.2% bovine albumin or sterile saline and inoculated directly into liquid or solid media.(40). Sputum culture used to detects 80% of TB cases with >98% specificity, sensitivity also high when compared to smear(culture needs 10-100 bacteria/millilitre of sputum),that allows species identification and drug susceptibility.There are Limitations in the smear technique that includes 28 slow culturing (takes 2-6 weeks); and that it needs specialised personnel, equipment, electricity and water. 3.In recent years, several molecular biologic techniques have been developed which decreases the time needs to identification of mycobacteria. newer methods include the polymerase chain reaction, which uses a heat stable DNA polymerase to amplify mycobacterial DNA from clinical samples . These methods include the polymerase chain reaction (PCR), which uses a heat-stable DNA polymerase to amplify mycobacterial DNA from clinical samples.. Some of the molecular biologic tests are as follows. Nucleic acid amplification (NAA) may represent significant improvement for TB diagnosis. Parts of M.tuberculosis genome are amplified and bound to a signal generating probe to allow detection. Tests based on NAA are rapid and usually highly specific for M.tuberculosis (close to 100%), with excellent sensitivity (>95% in smear positive, 60-70% in smear negative sputum specimens).42-44 Limitations of NAA tests include complexity and cost. Currently, NAA tests

are primarily used for confirmation of smear positive results or for primary case finding in combination with other methods. Ocular samples have also been analysed using NAA tests in a number of studies.There is a new assay in that uses viruses that infect mycobacteria to demonstrate the presence of M.tuberculosis that is Mycobacteriophage. This newer technology not yet widely available. other newer technologies used for TB diagnosis those are based on the detection of mycobacterial antigens.carbohydrate antigens (Lipoarabinomannan) and DNA both are released into the blood stream when the bacterium has lysed,those are filtered by kidneys and can be detected in urine . PCR has shown good sensitivity in preliminary studies for above antigens. The advantage of the above test includes easy collection of specimen, compared with sputum it has less generation of infectious aerosols and this test is not influenced by the immune status of the patient antigens

ANCILLARY DIAGNOSTIC TESTS:

The diagnosis of ocular tuberculosis is often made presumptive due to lack of ocular tissue for diagnostic purposes. Diagnosis is mostly made out from the clinical presentation and from few tests that shows the evidence of infection by the tubercle bacilli in the patient. The specific tests are tuberculin skin tests, chest radiography and IGRAs (Interferon Gamma Release Assays).

1.Radiography:

The characteristic lesions of Pulmonary tuberculosis are multi nodular parenchymal infiltrations that involves the apical and posterior segments of

the upper lobes and in the lower lobes superior segments are commonly involved. In cases where tuberculosis occurs in HIV infected patients, common finding is hilar adenopathy. In active pulmonary tuberculosis common findings are consolidation, cavitation, and satellite lesions which may lead to fibrosis, upward contraction,and volume loss. Pleural effusions are caused when tuberculosis involves the pleura which at times may be massive. When it involves the pericardium it causes pericardial effusions. In case of inactive pulmonary tuberculosis the findings will be peripheral calcified pulmonary nodules and/or calcified hilar lymph nodes which when occurs together is called as Ghonfocus/complex. Radiography thus can be used to differentiate active disease from a remote pulmonary tuberculosis, which can be used to substantiate the diagnosis of ocular tuberculosis. Sometimes there may not be any evidence available to demonstrate pulmonary infection in the setting of ocular and/or other extra pulmonary tuberculosis. Chest radiography is easily available, highly sensitive in HIV negative patients and convenient which are its advantages. On the other hand, disadvantages are highly non-specific and not reliable in HIV positive patients.

2. Blood cultures and serum antibody testing: In case of AIDS patients, routine blood sampling for smear and culture, a minimally invasive procedure which is advocated to diagnose disseminated mycobacterium. Serological tests as means of diagnosis is still under investigation and is not available routinely.

3. Tuberculin skin test (Mantoux) 4. Interferon Gamma Release Assays (IGRAs) QuantiferonTB Gold Assay. The last two are separately discussed below.

MANTOUX TEST

Mantoux test involves intra dermal injection of a polyvalent antigenic mixture of non-species specific molecules that are obtained from filtrates of sterilized, concentrated cultures that provokes a delayed hypersensitivity reaction, producing characteristic induration at the injection site the size of which is interpreted. The use of old tuberculin for the test is replaced by PPD-S (purified protein derivative), a standardized product which is prepared from mycobacterium tuberculosis by Siebert's method. The Mantoux test is the most commonly used test which serves as a diagnostic tool to detect exposure to mycobacterium tuberculosis. It is used extensively in epidemiological survey and in evaluating the patients with suspected active tuberculosis clinically. In treatment it plays a role in assessment of anti

tubercular drug therapy. The strength of the test dose of PPD-S is denoted in Tuberculin Units (TU). The dosage of PPD is 5 to 10 TU in developed countries and in case of developing countries like India, where tuberculosis is highly prevalent the recommended dose as per WHO guidelines is 1TU.

USE OF MANTOUX TEST :

1) Latent TB infection can be detected (future risk of development of the disease is correlated by considering the size of the mantoux reaction, so when there is increase beyond the cutting point it must be taken into account as one of the risk factors for the progression to disease).

2) Recent infection can be detected which will be evident from the conversion of the Mantoux from negative to positive.

3) As a part of the diagnosis of the TB disease which is done routinely.

READING THE MANTOUX REACTION

The area of induration in the forearm is measured transversely to its long axis which is recorded in millimetres. In case of positive reaction induration usually appears by 24hrs, reaching the maximum size around 72hrs. Reading of the reaction should be done as close as possible to 72hrs after the injection but, when this is not possible, reading from 48hrs to seven days is acceptable. Usually reading after 72hrs is of less-certain significance as their interpretation is not informed by epidemiological data. However, in case of positive reactions that develop after 72hrs, it should be considered as true positive.

TABLE-3

INTERPRETATION OF MANTOUX TEST AS PER AMERICAN THORACIC SOCEITY AND CDC

5mm or >	Positive in high risk individuals (abnormal CXR, Recent contacts, HIV, immuno suppression treatment for organ transplant, for cancer treatment, systemic that is prolonged (> 6weeks) and in a dose of prednisone > or = 15mg/day; the higher the dose greater the risk of reactivation of tuberculosis, end stage renal failure.
10mm or >	Positive in patients HIV- negative IV drug users, Low socio-economic background, medical conditions increasing the risk of TB, dose of prednisone <15mg/day long term, diabetes mellitus (including insulin dependent), alcoholism, malnutrition or disseminated malignancy.
15mm or >	Positive in individuals without any of the above said risk factors.

MANTOUX SKIN TEST IN TUBERCULOSIS UVEITIS:

Sensitivity : 65.8%

specificity : 45.8%

positive predictive value : 52%

REPEAT MANTOUX TEST

THE BOOSTER EFFECT

When the patient is previously sensitized to mycobacteria many years earlier, the first intra dermal injection of tuberculin shall produce a negative or weakly positive response due to the reason that there will be very few sensitized lymphocytes in the circulation which cannot produce a significant local response. When test is repeated, a larger reading may be obtained because, the response is being recalled or due to the booster effect of the first test.

The second reading obtained by booster effect is the correct one, which must be used for decision making or in future for comparison. Boosting effect will be maximal when

the second test is done between 1 to 5 weeks after the initial test, and it may

continue to be observed for up to 2 years.

The boosting phenomenon is often occurs in old age patients, or in case of infection by non-tuberculous mycobacteria or due to BCG vaccination which produces the

tuberculin sensitivity.

THE TWO STEP TEST

The two step test is done in patients who undergo serial mantoux tests to differentiate boosting effect from that of the conversion. It is performed when establishment of a true

Baseline Mantoux reaction is needed. The second test is required only when the initial reading is negative. A time interval of one week is required between first test and re-testing. As boosting phenomenon lasts up to two years, two step testing is unnecessary in a patient who has been tested in the preceding two years. The site of the two tests must not be the same as it can result in an increased reaction size. So sites must be different for interpretation.

Indications for Two-step testing are as follows, where serial mantoux

tests are to be used:

1) Health care workers - They are likely to be subjected to serial testing as part of tuberculin surveillance programmes, or after exposure to a TB case.

2) Before travelling to countries with high incidence rate although this is applicable only to those who are about to live or work in such contact for many months, or if they are at risk to have contact with people with TB there.

3) Two step test is unnecessary for the initial Mantoux test in people who are exposed to TB. Incase if their exposure to TB is significant then they will have already been boosted by the time the first test is done.

MANTOUX CONVERSION

MECHANISM

Boosting differs from conversion where boosting is a recall of the hypersensitivity reaction to the antigenic stimuli in the absence of new infection, in comparison to conversion where there is development of new or enhanced hypersensitivity reaction due to infection with mycobacterium tuberculosis or non tuberculous mycobacteria. BCG vaccination is also included in it.

DEFINITION

Mantoux conversion is defined as the change in Mantoux hypersensitive reaction that meets either of the following criteria:

- change from a negative reaction to a positive reaction.
- An increase in the size of the induration of >= 10mm.

THE INTERVAL BETWEEN MANTOUX TESTS IN THE CONTACTS OF TB

DISEASE:

Timing that is required for the immunological changes to occur for Mantoux conversion following infection is debatable. The children who are vaccinated with M.tuberculosis, develop a positive reaction in three to seven weeks time. Based on this, tuberculosis contacts are tested for the conversion, the second tuberculin test is done 8 weeks after the date of the last contact with the source

case of tuberculosis.

TESTING FOR CONVERSION IN PEOPLE WITH A DOCUMENTED MANTOUX RESPONSE:

Two tests for the conversion are not required in the case of a documented Mantoux result within the past 12 months. In the course of testing for conversion the prior documented pre-exposure results may be used as the baseline value. Positive reactions older than 12 months are invalid and cannot be used as a baseline because it may wane with time and therefore cannot be relied upon.

So, if a person has documented Mantoux test results, that falls within the period of past 12 months is exposed to infectious tuberculosis, only one

test is enough to detect the conversion. It must be done 8 weeks after the date of last exposure. This is applicable specifically to those people whose previous Mantoux result is prior BCG vaccination. The Mantoux reactivity of former cases will not wane to the same extent as above cases.

Former cases of tuberculosis disease when exposed to tuberculosis will not need Mantoux testing.

SIGNIFICANCE

Conversion is observed to be associated with an annual incidence of tuberculosis disease of 4% in case of adolescents or 6% in case of contact of smear-positive cases.

ACTION:

Persons who are positive for conversion must be investigated for tuberculosis disease. When requirement for full treatment is excluded, they must be considered for the treatment of latent infection.

When the Mantoux test reading increases between testing by 10mm and the second test also shows correct reading it must not be considered as a conversion. There may be a controversial situation where the second test may be positive but still the change in diameter of the induration does not meet the criterion for it to be termed as conversion. There will be a situation with a question of what to be done with these individuals.

There is no proper evidence to guide a decision about how to go about in this situation.

The recommendation of Ministry of Health's tuberculosis working group is that:

- A chest x-ray has to be done
- Treatment for LTBI should be given only in the following situation :

  - presence of risk factors for the tuberculosis infection to progress to disease; or

  - presence of close contact with a smear positive pulmonary case.

MANTOUX REVERSION

The change of a previous positive result to a negative one is termed as Mantoux reversion. This is an uncommon phenomenon in healthy individuals which is observed only in less than 10% of such people with a previous positive result. Reversion phenomenon is commonly occurs in the following :

1) Old age adults (estimated at 8% per year)
2) When the initial Mantoux reading < 14mm
3) In patients where the initial positive reaction obtained was a boosted result (detected by two-step testing).

ADVANTAGES OF MANTOUX:

1. Cheap and convenient .
2. Easily available.
3. In population where the BCG vaccination and NTM exposure is low, it is reliable.

DISADVANTAGES OF MANTOUX:

1) Low Specificity.
2) Proper injection technique to be followed.
3) Test is subjective.
4) Boosting effect is a disadvantage in interpretation.
5) BCG vaccination and NTM exposure results in high false positivity.
6) Second visit is necessary for interpretation.

False Negatives range from 17% - 29%

1) Increase in Age(old age)
2) Sarcoidosis, lymphoma, leukemia
3) Uraemia
4) Hodgkins disease

5) Corticosteroid use and other immunosuppressive used has an influence in mantoux test(prednisone >15mg/day, cyclophosphamide, methotrexate,and azathioprine etc)

6) Overwhelming tuberculous infection

7) Viral diseases like measles , mumps, HIV

8) Poor reactors intrinsically

9) Metabolic disorders like renal failures and diabetes mellitus in particular

FALSE POSITIVE

1) Atypical mycobacterial infections

2) Prior vaccinations with BCG

3) Health care workers

QUANTIFERON-TB GOLD IN TUBE ASSAY

INTRODUCTION

The Quanti FERON®- TB Gold IT test is a test for Cell Mediated Immune (CMI) responses to peptide antigens that simulate mycobacterial proteins. These proteins, ESAT-6, CFP-10 and TB7.7(p4), are absent from all BCG strains and from most non-tuberculosis mycobacteria with the exception of *M.*

*kansasii, M.szulgai*and *M.marinum.* Individuals infected with *M. tuberculosis* complex organisms usually have lymphocytes in their blood that recognise these and other mycobacterial antigens. This recognition process involves the generation and secretion of the cytokine, IFN-γ. The detection and subsequent quantification of IFN-γ forms the basis of this test.

Prevention of blindness due to ocular tuberculosis needs proper diagnosis and treatment.

ocular tuberculosis-criteria

1. Proper clinical findings
2. Relevant systemic investigations
3. Mantoux test
4. Empiric anti-tuberculosis treatment(positive response)

Presence of Mycobacterium tuberculosis bacilli or its DNA in aqueous or vitreous fluids/ ocular tissues and imaging. The highly sensitive and specific technique is PCR. The new upcoming diagnostic tools for tuberculous infections are molecular biology techniques for detection of M tuberculosis DNA and interferon-gamma release assays, those tests are improved the specificity of the diagnosis and the ability to ascertain exposure to the infectious agent .

POSTERIOR SEGMENT IMAGING

Fundus fluorescein angiography

Optical coherence tomography (OCT)

Indocyanine green angiography

The tuberculous lesions and their complications can be outlined by USG .Endoretinal biopsy specimens can be help in some cases . However, definition of case of tuberculosis vary in different countries or different regions of one country. extreme variations in clinical presentation and lack of diagnostic criteria will make the diagnosis of intra ocular tuberculosis is difficult. Moreover, many of the investigations are costly, invasive and inaccessible to most of the patients. Diagnosis of ocular tuberculosis in patients with HIV will be very difficult because absence of molecular or other diagnostic tests as PPD test may be negative due to energy. These patients should not be managed by ophthalmologists alone, They should be gets benefit from concomitant management by an infectious disease expert. There is no well defined criteria to diagnose intra ocular tuberculosis, although several attempts have been made to diagnose but those things couldn't provide a proper criteria . There are few guidelines for the diagnosis of intraocular tuberculosis, those are based on laboratory investigations and clinical parameters, follow-up examinations and therapeutic response to ATT.

SIGNS OF OCULAR TUBERCULOSIS

Presence of features of any of the following uveitis, cyclitis, choroiditis, retinitis ,retinal vasculitis, neuroretinitis optic neuropathy ,endophthalmitis, panophthalmitis clue to suggesting possible tubercular etiology-intractable disease course and un resolving to any treatment.

DIAGNOSTIC CRITERIA FOR TUBERCULAR UVEITIS

A. CLINICAL SIGNS

- Cellular reaction in the anterior chamber and or vitreous with or without postsynechiae
- Vitreous snow ball opacities in the inferior vitreous.
- Perivascular cuffing of inflammatory exudates.
- Solitary or multiple choroidal granulomas with or without exudative retinal detachment.
- Optic disc granuloma with or without neuroretinitis.
- Subretinal abscess

B. OCULAR INVESTIGATION

- Demonstration of AFB/culture of M.tuberculosis from the ocular fluids.
- PCR Positivity for ocular fluids IS6110 or other mycobacterium genome.

C.OTHER INVESTIGATIONS

- Mantoux reaction(POSITIVITY)
- Healed or active tubercular lesion on radiography of chest.
- Demonstration of tubercular granuloma/ Culture of M. tuberculosis /AFB (Evidence foe extra pulmonary tuberculosis)

D. THERAPEUTIC TEST

- A positive response to anti-tubercular therapy over a period of 4-6 weeks is highly suggestive of a possible tubercular etiology.

Any one or more of the clinical signs (A) with any of the ocular positive tests in (B) could be confirmatory of ocular tuberculosis. Any one or more of the clinical signs (A) with any of the positive corroborative tests in (C) or a positive therapeutic trial (D) could be considered suggestive of presumed ocular tuberculosis that would merit a full course of anti-tubercular treatment.

TREATEMENT OF TUBERCULOSIS

Treatment of tuberculosis has changed over the past decades. Tuberculosis remains a major health concern world wide and in developing countries. Hence a comprehensive strategy is promoted by world health organization, DOTS is the acronym for directly observed treatment, short course. It is the only strategy which has been documented to be effective world

wide on programme basis and is most widely used in India. A course of 4-drugs combination chemotherapy (isoniazid [INH], rifampicin, pyrazinamide, and ethambutol) for a period of 6 months has been advocated for systemic tuberculosis. Similar therapy is recommended for active ocular tuberculosis. Ethambutol is usually discontinued 2 months after initiation of therapy, and the remaining 3 drugs can be continued for next 4 months. This drug regimen has been found to be effective as the standard 9-month course. In adults with ocular tuberculosis, we use the combination of isoniazid 300mg orally per day, rifampicin 600mg orally per day, pyrazinamide 2g orally per day, and ethambutol 800mg orally per day. Pyridoxine 50mg orally per day should be given to prevent INH neurotoxicity. It is recommended that patients with ocular tuberculosis start on a minimum of 3 drugs for chemoprophylaxis.

Patients suffering from HIV infection and who are infected with M. tuberculosis should be treated with standard regimen. Children with active ocular tuberculosis may be treated with isoniazid 10 to 15mg/kg/d maximum dose of 300mg/kg/d), rifampicin daily dose of 10 to 20mg/kg/d (maximum dose of 600mg/kg/d), pyrazinamide daily dose of 15 to 30mg/kg/d(maximum dose of 2g/d), streptomycin 20 to 40 g/kg/day (maximum dose of 1g), and ethambutol 15 to 25mg/kg/d(maximum dose of 2.5g).

Topical therapy for tuberculous anterior uveitis consists of prednisolone acetate 1% eye drops and cycloplegics/mydriatics. Antiglaucoma therapy in the form of beta-blockers and carbonic anhydrate inhibitors may be given for

the patients with secondary glaucoma. Surgery for cataract and glaucoma can be performed if indicated when the inflammatory reaction is brought under control and the eye has been quite for a minimum of 3 months.

DRUG REGIMENS FOR TREATING INTRAOCULAR TUBERCULOSIS:

Treatment for ocular tuberculosis-drug regimens are same that of pulmonary and extra pulmonary tuberculosis. ocular involvement improves with systemic treatment.some studies described 9 months of chemotherapy with rifampicin and isoniazid will provide some improvement. Recommendation of CDC for the use of ATT is all the four drugs can be used (isoniazid, rifampicin, pyrazinamide, and ethambutol) for an initial 2-Month period and then followed by different Options over next 4 to 7 months for treatment of Tuberculosis . combinations with fixed dose of these agents have been tried. These combinations may reduce the bioavailability of the agents, even though these may be convenient for the patient. Drug resistance should be kept in mind. Patients with primary resistance to isoniazid is more than 4%, and patients who come from region with higher resistance to multidrug therapy, in whom the use of a 4 drug regimen should be followed by consultation with an internist who had better experience in the treatment of drug-resistant tuberculosis . Directly observed therapy should be used whenever possible. Patients who have findings suggestive of ocular

signs,mantoux positivity,positive sputum culture or other systemic findings of tuberculosis had to be treated with ATT.

Isoniazid, rifampin, ethambutol, and pyrazinamide are the drugs suggested by American thoracic society for pulmonary tuberculosis which is to be taken for 2 months (first line drugs). moxifloxacin 400mg orally once daily can be replaced for ethambutol contraindicated patients. Ethambutol is should be stopped after 2 months because of its side effects of optic neuropathy and ganglion cell loss. The other two drugs (Isoniazid and rifampin) should be taken for another -7 months for atotal period of 6-9 months, according to the effect of the drug. The end point and exact duration of treatment for ocular tuberculosis is not known. Tuberculosis at any site which shows slow response to therapy and intraocular TB patients require prolonged therapy for tuberculosis. Patients with uveitic inflammation showing ocular signs of TB with mantoux positivity with no systemic features and negative chest X RAY and lab results of tuberculosis have controversial management. If severe uveitic inflammation not responding to local immunesuppressive drugs or in patients with retinal vasculitis systemic immunosuppressive drugs can be given. Recurrent uveitis can be prevented by adding steroids to ATT for patients with latent tuberculosis. In TB uveitis topical corticosteroids can be added after it clearly responded to antibiotic therapy to reduce the ocular inflammation and to improve visual function. Oral corticosteroids are usually not required. Ocular tissue damage caused by delayed type hypersensitivity

can be limited by using Immunosuppressive Agents ,Low-dose systemic corticosteroids for 4 to 6 weeks, along with multidrug ATT. Monodrug therapy with corticosteroids alone shoud never be attempted as these favour bacilli multiplication which lead on to panophthalmitis,flaring up the latent tuberculosis infection and also cause poor visual out come, so steroids should always be accompanied by ATT.

Topical prednisolone and cyclopent eye drops are the preferred treatment for anterior uveitis in ocular tuberculosis patients. Topical beta blockers and carbonic anhydrase inhibitor can be given if the intra ocular pressure is elevated. Alpha agonists and prostaglandin analogues are not given in uveitis patients but can be used in case topical beta blockers and carbonic anhydrase inhibitors are not effective in controlling intra ocular pressure.Rifabutin should not be used in the treatment of oculat tuberculosis as it itself causes anterior uveitis.

APPROACH TO UVEITIS PATIENT WITH POSITIVE MANTOUX REQUIRING IMMUNE-MODULATORY AGENTS:

Patients treated with anti-TNF biological agents for anterior uveitis or any other auto immune diseases may have flaring up of latent tuberculosis infection.so,patients treated with anti-TNF agents should under go mantoux test.

The proposed treatment guidelines for latent tuberculosis (patients with mantoux positive) are:

Isoniazid 300 mg/day for duration of 9 months, the drug given twice weekly at a dose of 15 mg/kg when daily therapy is not possible. 2.Rifampicin should be given for a duration of 4 months daily when isoniazid is contraindicated, when the therapy duration must be confined to 2 months in that case rifampicin with pyrazinamide daily for 2 months is given. If the mantoux reaction to 5 tuberculin units of PPD is 10 mm OR 5 mm in HIV positive patients ,recent contact with an infective persons or chest x-ray showing evidence of old tuberculosis needs treatment irrespective of their age. Tuberculosis with HIV infection may complicate the effectiveness of ATT.

Tuberculosis that is resistant to isoniazid and rifampicin is known as MDR-TB. When tuberculosis is resistant to isoniazid and rifampicin and 3 or more of the 6 second line ATT drugs is known as extensively drug resistant tuberculosis (XDR-TB) which is an enormous global public heath problem. Development of drug resistant tuberculosis may be due to factors including poor compliance,improper drug regimen and physicians error in treatment or natural mutations or a combination of all these factors. combination of drugs with minimum of 3-4 additional ATT drugs for duration of 18-24 months is generally recommended. The additional ATT drugs are rifabutin, fluoroquinolones, interferon gamma and linezolid. immunocompromised patients with intraocular tuberculosis who are treated with highly active anti-

retroviral therapy reported with fast recovery of their CD count and also it increases the inflammatory response which leads to latent infection to become manifest . occasionally there may be occurance of severe systemic disease due to the immune recovery which is directed against the residual pathogens. Retinalamine is the drug which effectiveness for the treatment of tuberculosis chorioretinitis is under evaluation.

ETHAMBUTOL RELATED TOXICITY

The toxicity is rare if the daily dose does not exceed 15mg/kg. if the patient receives daily dose of 25mg/kg or more of ethambutol ,those will experience ocular toxicity that is also less than 2%.

The toxic effects of the drugs are red-green dyschromatopsia,optic neuritis, disc hyperaemia, disc oedema, peripapillary splinter hemorrhage, optic atrophy, scotomas, optic atrophy and foveal pigmentary changes. The mechanism of drug toxicity ,the drug disturbs the mitochondrial function through excitotoxic pathway and also the toxicity depends on mitochondrial homeostasis,decreased ATPase activity. The occurance of optic neuritis is usually abrupt and seen after 3-6 months of onset of treatmently. All patients who receives ethambutol should have their basic ophthalmic evaluation which includes visual acuity, colour vision, visual field. These patients should be examined regularly for every 2- weeks, and they should be followed up for every 3-6 months. If there is any side effects because of this ethambutol ,the drug should be stopped immediately and vision will improve within 10-15

weeks after the stoppage of the drug. Use of ethambutol in children should be avoided. If in case the vision doesn't gets improve, parentral hydroxycobalamine should be started. The dose is 0mg/day over a period of 10-28 week should be given. eventhough majority of symptoms can resolve over a period of 3-12 months ,permanent visual loss can occur.

DOTS 54

Directly Observed Treatment, Short Course (DOTS) Chemotherapy. Effective anti-tubercular drugs have been available for nearly 50 years. The cases are divided into two types of categories and it consists of an intensive phase and a continuation phase Treatment Categories and Sputum Examination Schedule

TABLE-9

Category of Treatment	**Type of Patients**	**T.B. Treatment Regimens**	
		intensive phase	continuation phase
CAT – I	New smear positive pulmonary tuberculosis New smear Negative pulmonary tuberculosis New extra pulmonary tuberculosis	$2H_3R_3Z_3E_3$	$4H_3R_3$
CAT – II	Relapse failure to respond on treatment after default Retreatment others	$2S_3H_3R_3Z_3E_3$ $+1H_3R_3Z_3E_3$	$5H_3R_3E_3$

TABLE-10

SIDE EFFECTS AND INTERACTIONS OF ANTITUBERCULOUS DRUGS

ANTI-TUBERCULAR DRUGS	SIDE EFFECTS	INTERACTIONS
Isoniazid	Neuropathy Increased in liver enzymes	Coumadin Benzodiazepines Theophylline
Ethambutol	Optic neuritis	None
Pyrizinamide	Increase uric acid Arthralgia	None
Rifampicin	Increase in liver enzymes Discolouration of secretions(urine becomes pinkish)	Inhibits effects of oral contraceptives, quinidine corticosteroids , coumadin, methadone, digoxin and oral hypoglycemic agents
.Streptomycin	Ototoxicity	Potentiates the action of neuromuscular blocking agents.
Rifabutin	Elevated liver enzymes	Anterior uveitis

PART - II

AIM OF THE STUDY:

- To evaluate the prevalence of ocular manifestations of tuberculosis in pulmonary TB patients, attending the CHEST MEDICINE OPD, Stanley medical college and hospital.
- To find out the manifestations of TB in eye, early definitive diagnosis and treatment for the same.

METHODS AND MATERIAL

STUDY DESIGN

- Cross sectional prospective study was undertaken on 167 sputum positive pulmonary tuberculosis patient attending the CHEST MEDICINE OPD was included in the study.
- Study period was from 2013 to till 2015

INCLUSION CRITERIA:

- Both adults and children
- Both male and female
- Patients with pulmonary TB

EXCLUSION CRITERIA

- HIV patients
- Other granulomatous disease.
- Ocular trauma
- Other systemic diseases

1. The importance of ocular examination in them was thoroughly explained in patients own language.

2. Consent in patients own language was obtained from all those who were willing to take part in study.

3. Any photographic records of the lesions were taken only if the patient consented for the same

4. Literature of approval attached.

ROUTINE OCULAR EXAMUNATION WAS DONE AS FOLLOWS:

- Ocular history
- Ocular examination included:

  Best corrected visual acuity.(Snellens chart)

  Slit lamp examination- Adnexa and anterior segment

  Dilated fundus examination (0.8%tropicamide +5%phenylephrine)

  90D and 20 D

  Neuro ophthalmological examination

  Orbit

  Schirmer's for dry eye evaluation

  FFA (when indicated) with the proper consent

Patients with suspected lesions were referred for complete systemic and laboratory work up

- Other investigations were done as per clinical indication included CT/MRI brain.

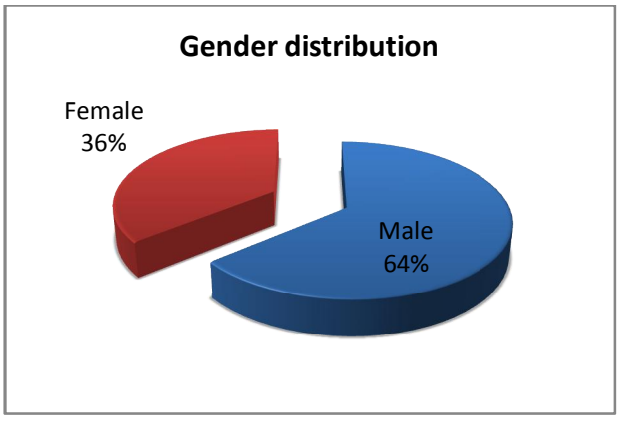
OBSERVATION

GENDER DISTRIBUTION:N=167

With no attempt to maintain an equal count of the gender population, we observed 64.07% males and 35.92 % females

TABLE 1

GENDER	NO OF PATIENTS	PERCENTAGE
Male	107	64.07%
Female	60	35.92 %
TOTAL	167	100%

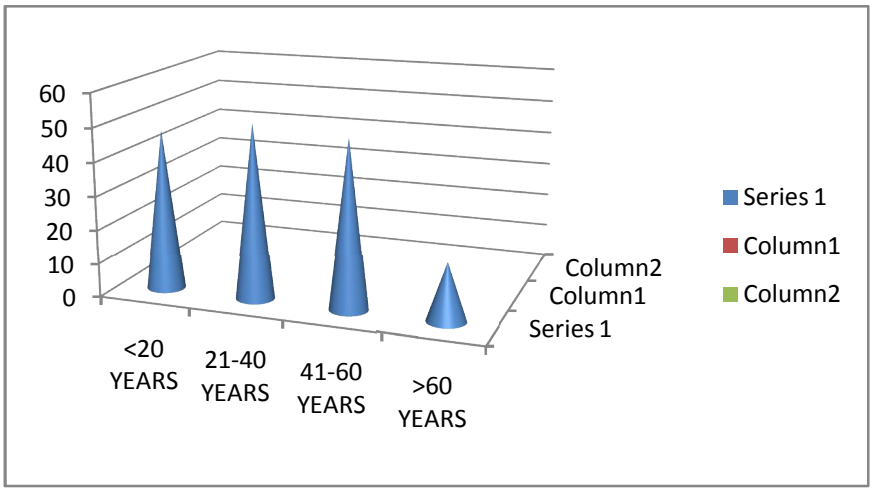


Maximum patients examined were male population, the higher the prevalence of tuberculosis in male population can attributed to the higher rate of exposure and hence the increased risk of contraction of infection.

TABLE 2

AGE DISTRIBUTION N=167

AGE	NUMBER OF PATIENTS	PERCENTAGE
<20	48	28.74%
21-40	52	31.13%
41-60	50	29.94%
>60	17	10.17%
TOTAL	167	100%

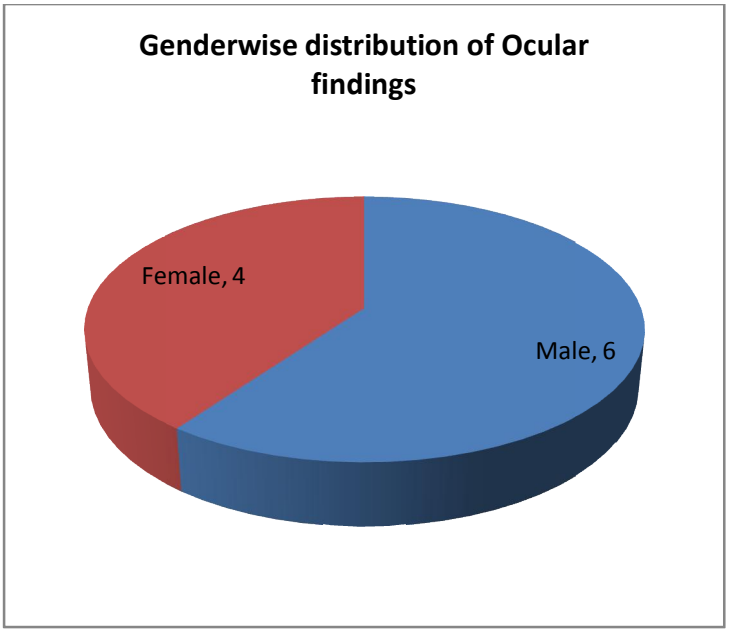


Maximum number of patients were examined in the age group between 21-40 and 41-60 years, which constituted to 31.13%, 29.94% of the study group.

TABLE-3

GENDER WISE DISTRIBUTION OF OCULAR FINDINGS

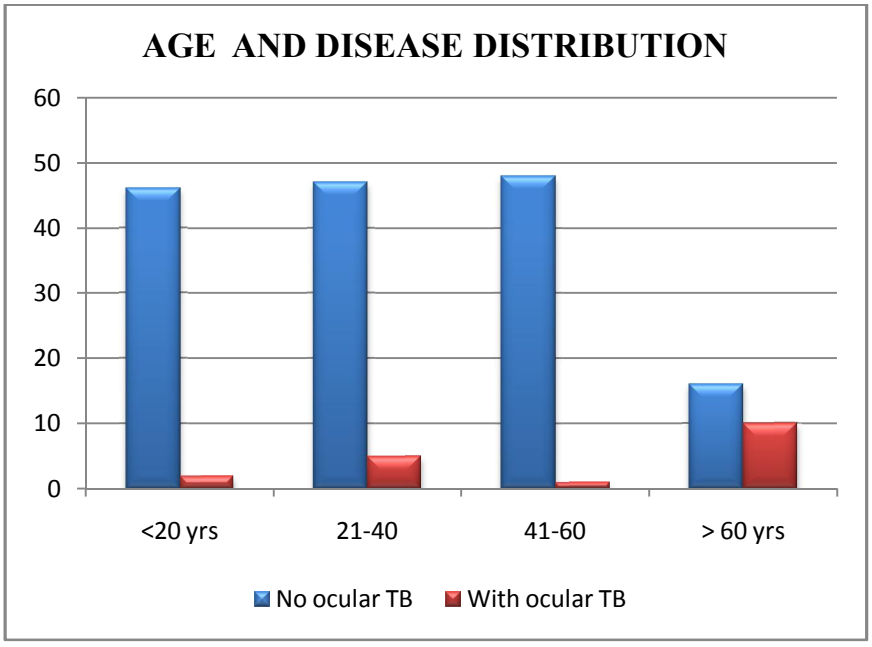
GENDER	NUMBER OF PATIENTS
MALE	6
FEMALE	4
TOTAL	10



Ocular finding also higher in male population can attributed to the higher rate of exposure.

TABLE 4

AGE AND DISEASE DISTRIBUTION		
Range	No Ocular TB	With Ocular TB
<20	46	2 (20%)
21-40	47	5 (50%)
41-60	48	2 (20%)
>60	16	1 (10%)
Total	157	10

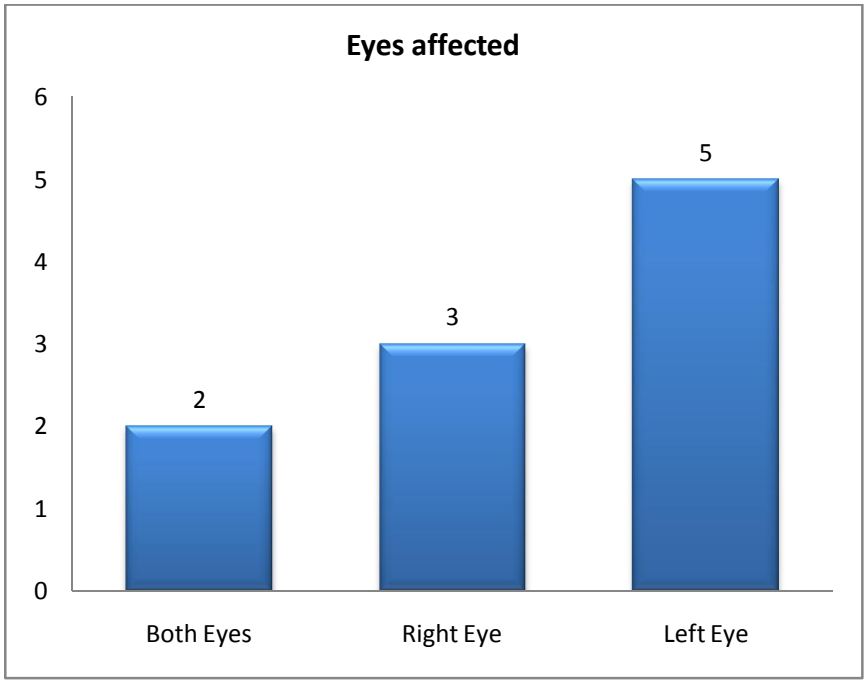


Maximum prevalence of ocular tuberculosis observed in the age group of 21-40 years,followed by 41-60 years

TABLE-4

Ocular involvement N=10

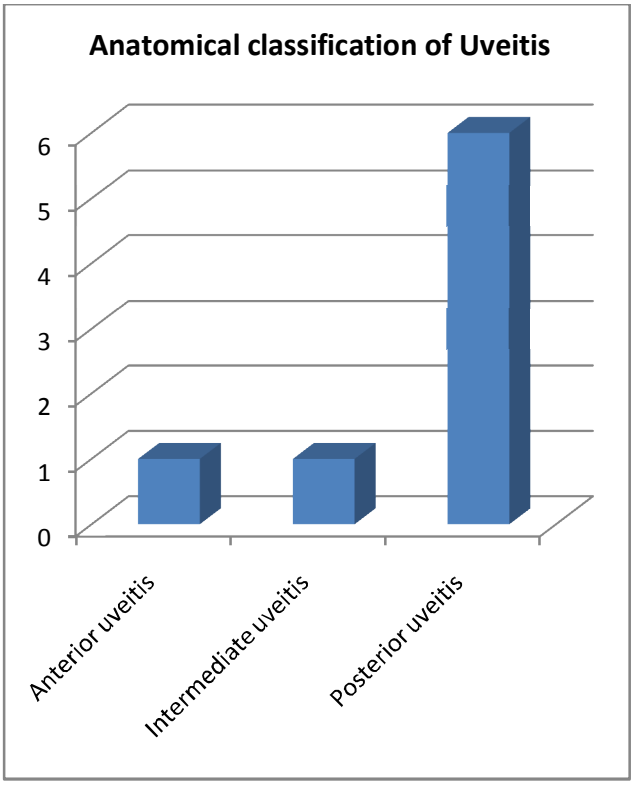
	Eyes affected	
	Both Eyes	2
	Right Eye	3
	Left Eye	5
	Total	10



Out of ten manifested cases eight showed unilateral involvement (80%),two showed bilateral involvement (20%). Maximum cases were unilateral involvement.

TABLE 5

Anatomical classification of Uveitis	
Anterior uveitis	1
Intermediate uveitis	1
Posterior uveitis	6

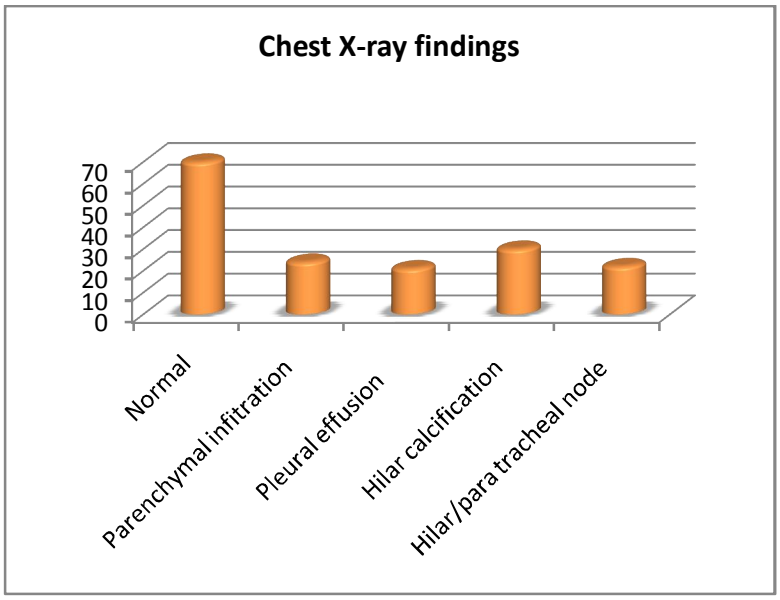


Out of the 8 uveitic cases,posterior uveitis constitutes N=6 (60%),Anterior uveitis N=1(10%),intermediate uveitis N=1(10%). According to anatomical classification of uveitis, majority of patients had posterior uveitis. in our study the most common ocular finding is choroidal tubercle.

TABLE 6

Radiological findings:(chest x-ray)

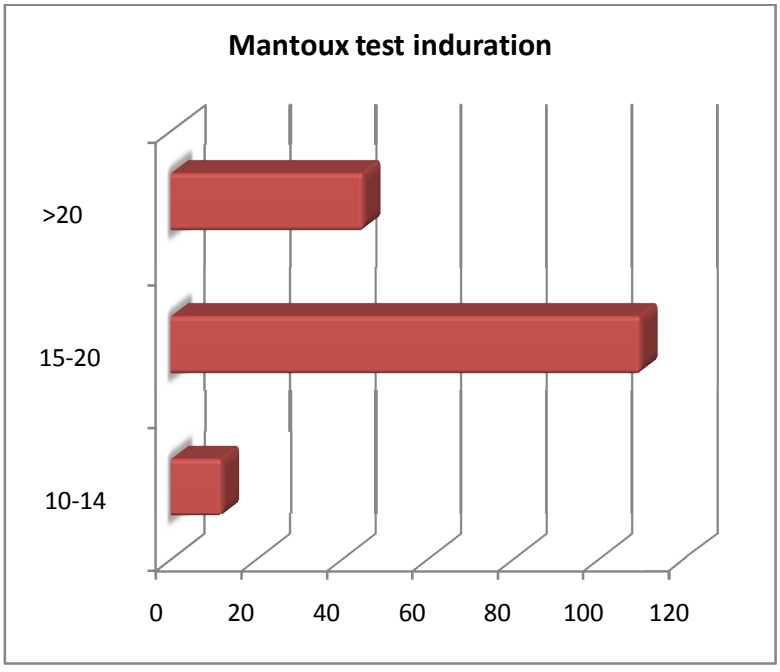
CHEST XRAY FINDING	NUMBER	PERCENTAGE
Normal	70	41.91%
Parenchymal infiltration	24	14.37%
Pleural effusion	21	12.57%
Hilar calcification	30	17.96%
Hilar/para tracheal node	22	13.17%
TOTAL	167	100%



All the patients in the study group were sputum positive pulmonary tuberculosis. Chest Xray was done in 167 patients. Chest X-ray revealed 70 (41.91%) patients with normal chest x-ray, 24 (14.37%) patients had parenchymal infiltration, 21 (12.57%)had pleural effusion, 30(17.96%) had hilar calcification. Rest of the 22(13.17%) patients had paratracheal nodes. Among the chest involvement, hilar calcification had the maximum perentage.

TABLE 7

Mantoux test induration	NUMBER	PERCENTAGE
10-14	12	7.18%
15-20	110	65.86%
>20	45	26.94%
TOTAL	167	100%

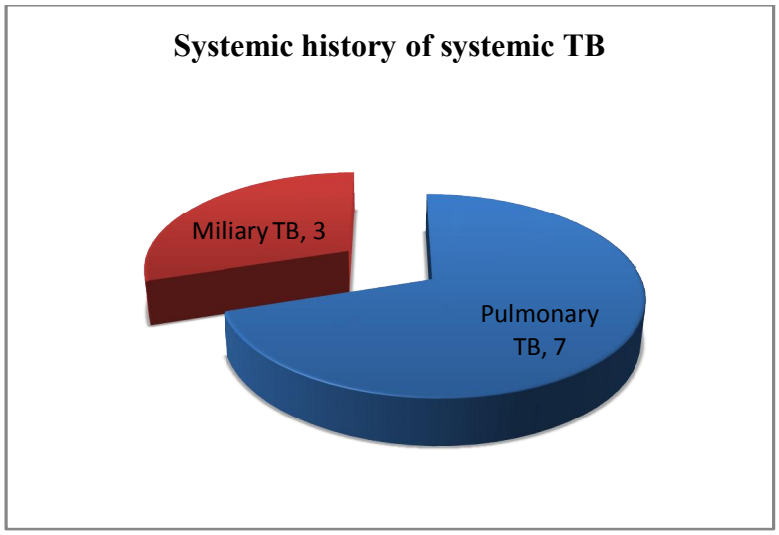


Among the 167 patients, 12 (7.18%) patients had induration of 12-14 mm, 110 (65.86%) patients had 15-20 mm, and the rest 45 (26.94%) patients had more than 20 mm. In this, Maximum patients had 15-20 mm induration.

TABLE 8

TUBERCULOSIS STATUS: N=10

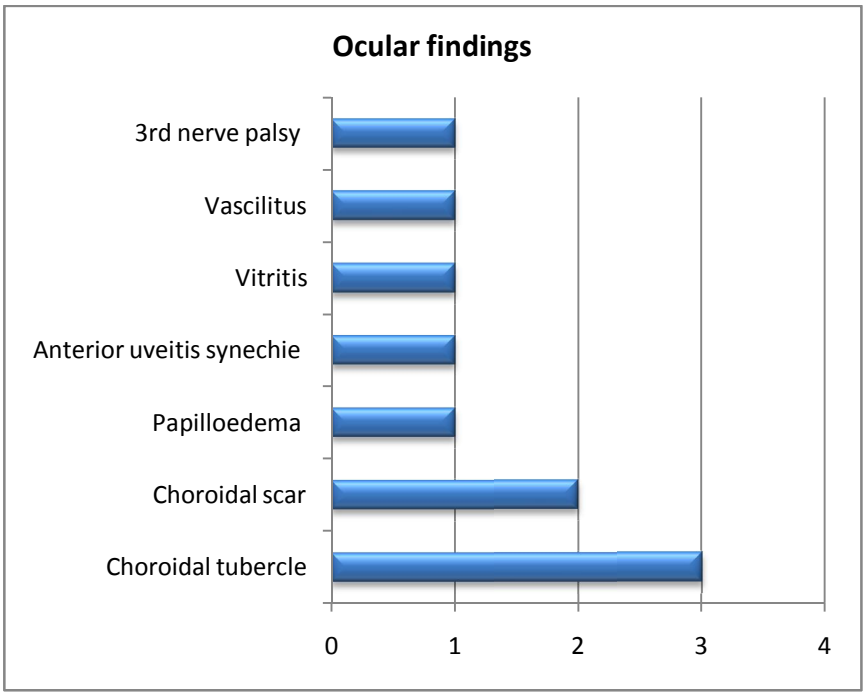
SYSTEMIC HISTORY OF TB	
Pulmonary TB	7
Miliary TB	3
Total	10



Three out of ten patients were diagnosed as miliary tuberculosis.Seven out of ten patients were diagnosed as pulmonary tuberculosis.

TABLE 9

OCULAR FINDINGS	NUMBER
Choroidal tubercle	3
Choroidal scar	2
Anterior uveitis	1
Vitritis	1
Vascilitus	1
Papilloedema	1
3rd nerve palsy	1
TOTAL	10

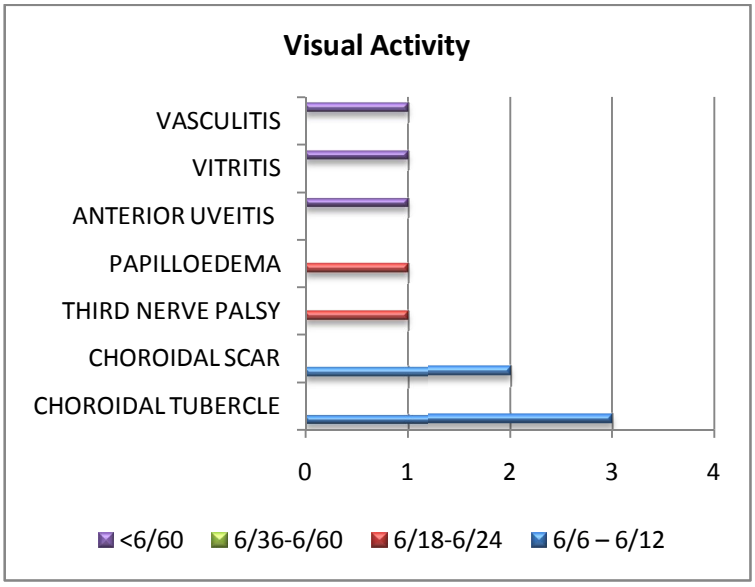


Ten out of one sixty seven patients had tuberculosis related ocular manifestations. Majority of patients in our study had choroidal tubercles(N=3) at the time of examination.

TABLE 10

VISUAL ACUITY AT THE TIME OF SCREENING

DIAGNOSIS	VISUAL ACUITY			
	6/6 – 6/12	6/18-6/24	6/36-6/60	<6/60
CHOROIDAL TUBERCLE	3			
CHOROIDAL SCAR	2			
THIRD NERVE PALSY		1		
PAPILLOEDEMA		1		
ANTERIOR UVEITIS				1
VITRITIS				1
VASCULITIS				1



Most of the patients were asymptomatic at presentation, some of the patients had decreased visual acuity. Vitritis, vasculitis and anterior uveitis patients had decreased visual acuity.

OCULAR SYMPTOMS: N:1O

OCULAR SYMPTOMS	NO OF PATIENTS
PRESENT	3
ABSENT	7

OCULAR FINDINGS:N=167

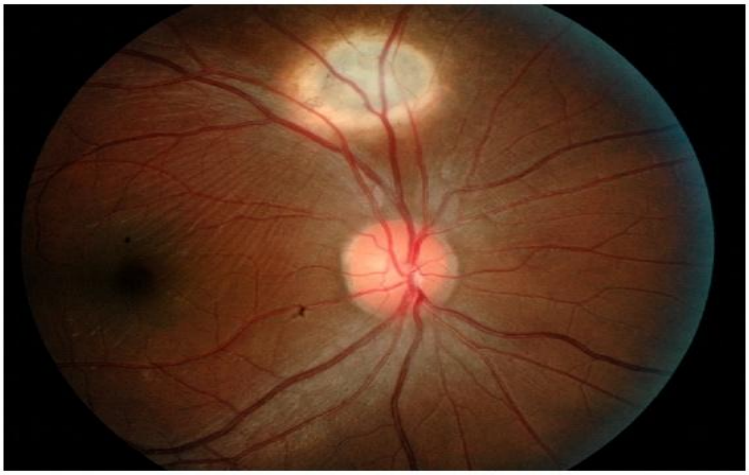
OCULAR FINDINGS	NO OF PATIENTS
PRESENT	10
ABSENT	140

OCULAR FINDINGS	OCULAR SYMPTOMS		TOTAL
	PRESENT	ABSENT	
PRESENT	3	7	10
ABSENT	0	157	157
TOTAL	3	164	167

Among the ten patients with ocular manifestations of tuberculosis, three patients presents with symptoms in the first presentation.

CHOROIDAL TUBERCLE

CHOROIDAL SCAR

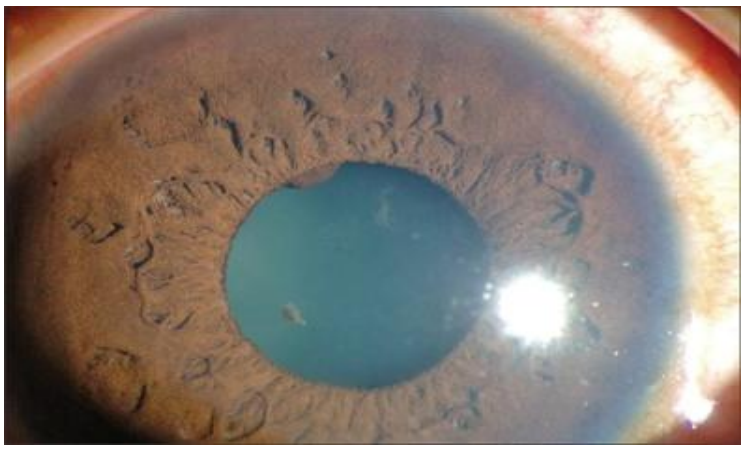


The above two findings are the most common ocular manifestations of active pulmonary tuberculosis.

RETINAL VASCULITIS

Sheathing of vessels noted in patients with active pulmonary tuberculosis.

ANTERIOR UVEITIS

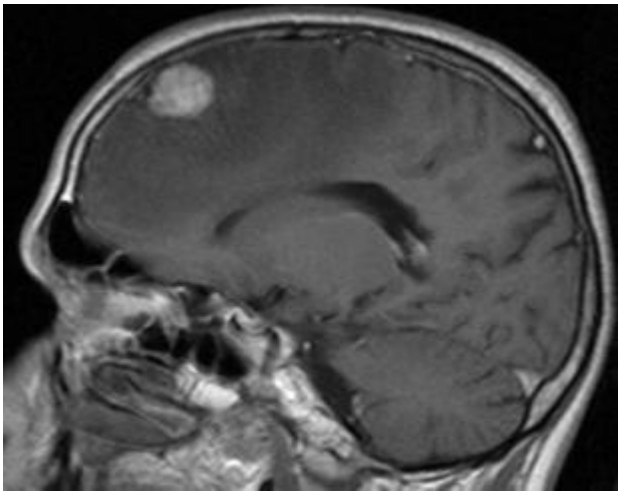


Anterior uveitis with posterior synechiae

PAPILLOEDEMA

Miliary tuberculosis can cause tuberculous meningitis, and raised intar cranial pressure it will lead on to papilloedema.

TUBERCULOMA



Tuberculoma of brain most commonly associated with miliary tuberculosis, it can lead on to cranial nerve palsies.

MILIARY TUBERCULOSIS

Ocular findings are most commonly seen in miliary tuberculosis patients.

DISCUSSION

AGE AND DISEASE DISTRIBUTION:

AGE	G.N.SAHU ET AL	PRESENT STUDY
N	55	167
<20	40%	28.74%
21-40	**43%**	**31.13%**
41-60	16.36%	29.94%
>60	NA	10.17%

- ✓ Majority of the patient prevalence in our study fell under the age group of 21-40 years followed by 41-60 years .this pattern was similarly noted in G.N.Sahu et al
- ✓ Biswas et al study showed with most TB patients belonging to the economically productive age group (15 to 54 years old)
- ✓ G.N.sahu et al showed maximum patients were at the age group of 21-40 years.
- ✓ Bounz et al study showed mean age is 37.6 plus or minus 14.7 yrs. However our prevalence rate of 31.13% is closely comparable with G.N.sahu et al study.
- ✓ Leon paolo et al showed maximum patients were at the age group of 41-70 yrs.

DISEASE DISTRIBUTION:

AGE	DISEASE DISTRIBUTION	
	G.N.SAHU STUDY	OUR STUDY
<20YRS	10%	40%
21-40YRS	**50%**	**43%**
41-60YRS	30%	16.36%
>60YRS	10%	NA

- ✓ Regarding the age wise disease distribution , 50% of the cases were between 21-40 years of age followed by 30% of cases were between 41-60yrs which is comparable with the G.N.sahu et al study.

GENDER DISTRIBUTION:

GENDER	BOUZA ET AL	SHARMA ET AL	OUR STUDY
N	100	100	167
MALE	85%	62%	64.07%
FEMALE	35%	38%	34.92%

- ✓ Our study shows a higher male prevalence in comparison to females. This finding was similarly noted in Sharma et al study.
- ✓ **"**Global variation and pattern changes in theepidemiology of uveitis"94. distribution is comparable with the results of the article was 62.2% male and37.8% female.

GENDER WISE DISEASE DISTRIBUTION:

GENDER	BOUZA ET AL	OUR STUDY
OCULAR INVOLVEMENT	18	10
MALE	14	6
FEMALE	4	4

- ✓ In our study shows higher male prevalence in comparison to females.This finding is similarly noted in bouza et al study.

LATERALITY AND THE DISEASE DISTRIBUTION:

- ✓ Regarding the laterality , in our study about 8o% of patients had unilateral and rest had bilateral (20%)involvement.
- ✓ When compared with the G.N sahu study it states that Both ocular and orbital tuberculosis are usually unilateral.
- ✓ In leon paolo et al study shows that maximum cases were unilateral involvement.

Visual acuity at presentation:

Visual acuity	Patients with Ocular Involment
6/6-6/12	**5**
6/18-6/24	**2**
6/36-6/60	**NIL**
Less than 6/60	**3**

- ✓ In our study showed that decreased visual acuity seen in 3 patients all the others were aymptomatic.
- ✓ Bouza et al study showed ,maximum cases were asymptomatic presentation.

PATHOLOGY OF THE DISEASE AND ITS DISTRIBUTION:

CLINICAL FINDINGS	BISWAS ET AL	BOUZA ET AL	LEON PAOLO ET AL	OUR STUDY
choroidal tubercle		12 (66.66%)	3 (42.85%)	3 (30%)
Choroidal scar	50%	8 (44.44%)	NA	2 (20%)
Vitritis		2 (11.11%)	NA	1 (10%)
Vasculitis		2 (11.11%)	2 (28.57%)	1 (10%)
Anterior uveitis		1 (5.55%)	2 (28.57%)	1(10%)
Papilloedema		NA	NA	1 (10%)
3rd nerve palsy		NA	NA	1 (10%)

- ✓ Regarding the pathology ,patients with choroidal tubercle N=3 (30%), choroidal scar N=2(20%), Vasculitis N=1(10%),anterior uveitis N=1(10%),vitritis N=1(10%) papilloedema N=1(10%),3RD nerve palsy N=1(10%)

- ✓ In our study the most common manifestation of ocular tuberculosis in patients with pulmo- nary tuberculosis is choroidal tubercle and choroidal scars.

- ✓ Biswas J et al study showed**,** The most common ocular finding was healed focal

  choroiditis (50%). There was no cases of Eales disease in that series .

- ✓ Bouza et al study revealed that 18% of cases with ocular findings in 100 proven pulmonary tuberculosis patients. He that posterior uveitis (choroidal tubercle and choroidal scars) more common among the culture positive patients.

- ✓ Sheu et al in this study he found that posterior uveitis is common among the culture positive patients. because choroid and ciliary body have the high oxygen tension.

- ✓ (Olazabal, 1967), this study showed that dissemination occurs through the caseous pulmonary lesion that erodes into the blood vessels or the lymphatic channels ,uveitis in ocular tuberculosis presents with a smouldering, insidious, progressive form .

Radiological evidence:

- ✓ According to radiological evidence hilar calcification=30(17.96%) parenchymal infiltration=24(14.37%) pleural effusion N=21(12.57%) hilar/para tracheal enlargement of nodes =22(13.17%) normal N=70(41.91%)

- ✓ The result is comparable with the G.N.SAHU ET AL study, which shows maximum chest involvement in tuberculosis patient is hilar calcification (18.8%).

- ✓ 70 Patients (41.91%),the x-ray chest was normal but all are sputum positive and higher limit of ESR.

- ✓ 97 patients (58.09%) chest x-ray suggestive of tuberculous etiology

- ✓ In that 97 patients 3 patients had miliarytuberculosis, in that choroidal tubercle(N=1), papilloedema (N=1),3RD nerve palsy (N=1)

MANTOUX REACTION:

REACTION SIZE	**G.N.SAHU ET AL**	**OUR STUDY**
10-14mm	5.45%	7.18%
15-20mm	50.90%	65.86%
>20mm	43.63%	26.94%

- ✓ In our study, mantoux reaction with 15-20mm maximum seen in 65.86% which is compared with G.N.SAHU ET AL study.

TREATMENT FOR THE DISEASES:

- ✓ Among the 10 patients all of them were received ATT on additional to it, choroidal tubercle N=3(30%), choroidal scar N=2(20%)treated with systemic steroids. Anterior uveitis N=1(10%) treated with topical steroids , vitritis N=1(10%) and vasculitis N=1(10%) both topical and systemic steroids. papilloedema and 3rd nerve palsy treated with ATT.

- ✓ A review by Gupta et al, 2007 updated the clinical spectrum, laboratory investigation, and diagnostic criteria that would assist in the diagnosis of presumed or confirmed intraocular TB so that anti-tuberculous therapy (ATT) can be initiated on a rational basis.

- ✓ Darrell et al, 1986, in miliary tuberculosis there will be small multipla choroidal tubercles will be present, active tubercles well respond to ATT ,it will take -6 months to resolve.after healing it will produce healed pigmented scar.

PREVALENCE OF OCULAR TUBERCULOSIS

STUDIES	PREVALENCE
BOUZA ET AL	**18%**
BISWAS ET AL	**1.39%**
LEON PAOLO ET AL	**6.8%**
OUR STUDY	**5.98%**

In our study, the prevalence rate is 5.98% which is comparable with the leon paolo et al study, The rate is higher the other studies.

CONCLUSION

- ✓ Mycobacterium *tuberculosis* can cause a wide spectrum of diseases in eye. The clinical diagnosis of ocular tuberculosis is not always easy because the manifestations in the eye are protean and can mimic other conditions. This makes the ophthalmologist relay on various other investigations to confirm the clinical diagnosis.
- ✓ Infected end organs typically have high regional oxygen tension (apices of the lungs ,kidneys, bones, meninges, eye, and choroid). M.tuberculosis tends to grow successfully in the choroid and ciliary body where the oxygen tension is high compared with other ocular structures.
- ✓ With the introduction of DOTS, the morbidity has decreased and the life expectancy of the patients have significantly increased. however the ocular manifestations still persists.
- ✓ Most of the patients are asymptomatic in that most common involvement is posterior uveitis.
- ✓ With the number of ocular findings observed, our study highlights the need for ocular screening in active pulmonary tuberculosis.
- ✓ We have only taken the pulmonary tuberculosis patients for screening, still many of the cases are their for examination like relapse and failure cases.

- ✓ Ocular TB may occur at both primary and secondary stage of clinical disease, patients may range in age from childhood to adulthood. virtually all ocuar and orbital diseases are a results of hematogenous spread.
- ✓ In this study most of the patients were in the age group of 20-60 years.HIV, ocular trauma, other retinal diseases, and other systemic diseases has excluded.
- ✓ The male gender had a preponderance(64.07%) over the female(34.92%)
- ✓ The diagnosis of ocular tuberculosis is always based on the combination of relevant history,clinical examination, investigations and sometimes a favourable response to therapeutic trial of anti tuberculosis therapy also.
- ✓ All this indicates ocular screening is necessary in active pulmonary tuberculosis.proper ocular screening of pulmonary tuberculosis patients will eliminates the preventable blindness.this can be made possible with adequate resourses and trained ophthalmic personnel.
- ✓ The prevalence of our study is 5.98% which is comparable with the studies.it can expand the knowledge base regarding the epidemiology of ocular tuberculosis and can contribute to awareness on the condition.

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PROFOMA

PARTICULARS OF PATIENT:

1.NAME: 6.INCOME:

2.AGE: 7.RESIDENCE:

3.SEX: 8.HOSPITAL REG:

4.RELIGION: 9.D.O.A:

5.OCCUPATION:

CLINICAL HISTORY:

1.COMPLAINTS:

2.HISTORY OF PRESENT ILLNESS:

3.PERSONAL HISTORY:

4.FAMILY HISTORY:

OPHTHALMIC EXAMINATION: RE LE

1.EYEBROWS:

2.EYELIDS:

3.EYELASHES:

4.CONJUNCTIVA:

5.CORNEA:

6.SCLERA:

7.ANTERIOR CHAMBER:

8.IRIS:

9.PUPIL:

10.LENS:

11.FUNDUS:

12.VISION:

13.OCULAR MOVEMENTS:

14.ORBIT:

15.SLIT LAMP EXAMINATION WITH 90 D:

16.FFA:

DIAGNOSIS:

TREATMENT

தகவல் வடிவம்

தலைப்பு : காசநோயினால் கண்ணில் ஏற்படும் அறிகுறிகளை கண்டறியும் ஆய்வு

பங்கு பெறுபவரின் பெயர் :

பங்கு பெறுபவரின் எண் :

மேலே குறிப்பிட்ட ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டது.

இதில் எனது கண்களை பரிசோதித்து, அதில் காசநோயின் அறிகுறிகளை ஆராய நான் முழுமனதுடன் தன்னிச்சையாக சம்மதிக்கிறேன்.

எந்த காரணத்தினாலே, எந்த கட்டத்திலும், எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவவ்வாய்வில் இருந்து விலகிக் கொள்ளலாம் என்று அறிந்துக் கொண்டேன்.

இதில் மருத்துவர் என் மீது எந்த ஊசியே, பங்கேற்பவர்கள் பாதிக்கப்படும் பரிசோதனையோ (invasive Diagnostic Test) செய்யப்போவதில்லை என்று அறிந்துக் கொண்டேன்.

இந்த ஆய்வு சம்மந்தமாவே, இதை சார்ந்து மேலும் ஆய்வு மேற்க்கொள்ளும் போதும், இவ்வாய்வில் பங்குபெறும் மருத்துவர் என் மருத்துவ அறிக்கைகளை பார்க்க என் அனுமதி தேவையில்லை. இதன் மூலம் கிடைக்கும் தகவல்களையும், பரிசோதனை முடிவுகளை பார்ப்பதற்க்கும், பயன்படுத்துவதற்கும் முழுமனதுடன் சம்மதிக்கிறேன்.

எனக்கு கொடுக்கப்பட்ட அறிவுரைகளின்படி நடந்துக் கொள்வேன். எதிர்பாராத வழக்கத்திற்கு மாறான நோய் அறிகுறி

தென்பட்டால் அதை மருத்துவரிடம் தெரிவிப்பேன்.இந்த ஆய்வில் நான் தன்னிச்சையாக தான் பங்கேற்கிறேன்.

இந்த ஆய்வில் எனக்கு தேவையான அனைத்து பரிசோதனைகளையும் செய்துக் கொள்ள முழுமனதுடன் சம்மதிக்கிறேன்.

மேலும் இந்த ஆய்வில் என்னையும், என் கண்ணில் உள்ள பிரச்சனைகளையும் புகைப்படம் எடுக்க முழுமனதுடன் சம்மதிக்கிறேன்.

பங்கேற்பவரின் கையொப்பம் / கட்டைவிரல் ரேகை

நாள்

நான், இவ்வாய்வை பற்றி அனைத்து விவரங்களையும் மேற்குறிப்பிட்ட நபர் புரிந்துகொள்ளும்படி அவருக்கு தெரிந்த மொழியில் எடுத்துக்கூறி சம்மதம் பெற்றுள்ளேன்.

ஆய்வாளரின் பெயர் மற்றும் கையொப்பம்

நாள்

ABBREVATIONS

1.AFB-ACID FAST BACILLI

2.AM-ALVEOLAR MACROPHAGE

3.TH-T HELPER CELLS

4.TNF-TUMOUR NECROSIS FACTOR

5.AIDS-AUTO IMMUNE DEFICIENCY SYNDROME

6.PCR-POLYMERASE CHAIN REACTION

7.NUCLEIC ACID AMPLIFICATION

8. IGRAS - INTERFERON GAMMA RELEASE ASSAYS

9. PPD-PURIFIED PROTEIN DERIVATIVE

10. TU-TUBERCULIN UNITS

11. CMI-CELL MEDIATED IMMUNITY

12. INH- ISONIAZID

13. MDR-MULTI DRUG RESISTANT

14. XDR-TB -EXTENSIVELY DRUG RESISTANT TUBERCULOSIS

15.DOTS- DIRECTLY OBSERVED SHORT COURSE TREATMENT

KEY TO MASTER CHART

1.NAME OF THE PATIENT

2.AGE

3.SEX

4.OP.NO

5.EYES AFFECTED

RIGHT EYE-RE

LEFT EYE-LE

BOTH EYES-BE

6.OCULAR FINDINGS

A.CHOROIDAL TUBERCLE

B.CHOROIDAL SCAR

C.ANTERIOR UVEITIS

D.VITRITIS

E.VASCULITIS

F.PAPILLOEDEMA

G.3RD NERVE PALSY

7.MANTOUX EXAMINATION

1.10-14MM

2.15-20MM

3.>20MM

8.CHEST XRAY FINDINGS

A:NORMAL

B:PARENCHYMAL INFILTRATION

C:PLEURAL EFFUSION

D:HILAR CALCIFICATION

E:HILAR/PARATRACHEAL ENLARGEMENT OF NODES

9.YEAR OF EXAMINATION

10.VISUAL ACUITY AT THE TIME SCREENING

15:6/6-6/12

16: 6/18-6/24

17:6/36-6/60

18:<6/60

1	2	3	4	5	6	7	8	9	10	11
1	Mahalakshmi	19	F	75518	LE		3	a	2015	15
2	Raja	30	M	220892	LE		2	a	2014	15
3	Lakshmi	34	F	299637	BE		3	a	2014	15
4	Selvaraj	56	M	220897	LE		2	e	2015	16
5	Sickhandar	54	M	220820	LE		2	e	2014	15
6	Pachiammal	56	F	127555	LE		3	a	2014	15
7	Selvi	37	F	99318	BE		2	e	2015	16
8	Annamalai	39	M	299737	RE		1	e	2014	15
9	Shanthi	34	F	237654	LE	F	2	a	2015	16
10	Victoria	20	F	91561	LE		2	a	2014	16
11	Saroja	38	F	62597	LE		1	e	2015	15
12	Francis	52	M	30166	RE		2	e	2014	16
13	Priyamma	49	F	305937	LE		3	e	2014	15
14	Fathima	16	f	326182	LE		2	e	2015	15
15	Kannapa	60	M	305208	BE		2	a	2014	15
16	Devaki	42	F	304559	RE		2	e	2014	15
17	kathirvel	41	M	19935	LE		2	e	2014	16
18	ganga	52	F	272389	LE		3	e	2015	16
19	ponnusamy	31	M	271670	LE		2	a	2014	15
20	dhandavarayan	60	M	24207	RE		1	d	2014	16
21	kanniamma	49	F	304003	LE		2	d	2015	15
22	raju	32	M	303981	LE		2	d	2014	16
23	sivagami	36	F	30400	RE		2	a	2014	16
24	pichumuthu	64	M	301862	RE		2	a	2015	15
25	nadeshan	39	M	86174	LE		2	d	2014	17
26	muniraj	32	M	295320	LE	A	3	a	2014	15
27	rajalakshmi	23	F	38181	LE		2	d	2015	15
28	papathi	46	F	67521	RE		3	d	2014	16
29	kannan	43	M	60872	LE		2	a	2014	16
30	kagan	34	M	387000	RE		2	d	2015	15
31	janaka	32	F	11863	RE		2	a	2015	15
32	mani	49	M	60072	LE		2	d	2014	15
33	sambath	46	M	54906	RE		2	d	2015	16
34	palayam	52	M	28617	LE		2	d	2014	15
35	madhumith	42	F	225150	LE	E	2	e	2014	18
36	merabeam	27	F	75108	LE		2	a	2014	17
37	ponnusamy	38	M	307988	RE		2	d	2015	16
38	meena	27	F	303991	LE		2	a	2014	15
39	raman	31	M	801672	RE		2	d	2014	15
40	mohan	32	M	61437	LE		2	d	2015	16
41	kuppuamy	43	M	77810	LE		2	a	2014	17

1	2	3	4	5	6	7	8	9	10	11
42	ramachandran	52	M	802613	RE		2	a	2014	15
43	vellaiyam	43	M	87255	LE		3	d	2015	16
44	mani	22	M	303989	LE		2	a	2014	15
45	valli	40	F	304001	LE		2	d	2014	16
46	thomas	17	M	297808	LE	B	2	a	2015	15
47	sumathi	25	F	304000	RE		2	a	2014	15
48	kaveri	43	F	301691	LE		2	d	2014	16
49	lalitha	32	F	321611	LE		2	d	2014	15
50	chellapan	53	M	90254	RE		2	a	2014	17
51	ponnusamy	44	M	206211	LE		2	d	2014	17
52	apparav	60	M	10923	RE		2	a	2014	15
53	ramalu	46	M	65891	LE		2	a	2014	16
54	govindhasamy	62	M	230674	LE		2	d	2014	17
55	kamala	53	F	32710	RE		3	d	2014	15
56	ramabai	55	F	123202	RE		2	a	2014	16
57	marry	26	F	143560	LE		2	d	2014	17
58	latha	30	F	69312	RE		3	a	2014	15
59	suresh	24	M	94332	LE		3	d	2014	16
60	maiammal	52	F	238501	BE	A	3	e	2014	15
61	muthualagu	33	M	15525	LE		2	a	2014	15
62	vijalakshmi	42	F	154466	RE		2	c	2015	16
63	kasthuri	39	F	82412	RE		2	c	2014	15
64	pupathi	56	F	467182	LE		2	a	2014	15
65	kasi	61	M	642311	LE		2	a	2014	16
66	praimala	63	F	110788	RE		2	a	2014	15
67	sundari	42	F	963170	RE		3	c	2015	15
68	arun	17	M	701761	LE		2	c	2014	17
69	jayaprakash	53	M	701894	RE		2	a	2014	15
70	samuvel	39	M	330461	LE		2	a	2014	15
71	eddy	45	M	381864	LE		2	a	2014	15
72	monakaran	22	M	825185	RE		2	c	2014	15
73	devaki	19	F	826519	RE		2	c	2014	15
74	nazir	40	M	129816	LE		2	c	2014	17
75	chandrasekar	12	M	826113	LE		2	a	2014	15
76	maniammma	43	F	624176	RE		2	a	2014	15
77	panju	11	F	825299	RE		2	c	2014	17
78	agasthus	49	F	65388	RE		3	c	2014	15
79	kathirvel	27	M	94264	LE		2	a	2014	15
80	dharani	17	F	23724	LE		2	c	2015	15
81	minan	18	M	82805	RE		2	a	2015	15
82	georgereddy	56	M	56489	RE		2	c	2015	15

1	2	3	4	5	6	7	8	9	10	11
83	yesudas	15	M	19004	LE		2	c	2014	15
84	saroja	45	F	49955	RE		2	a	2014	17
85	balan	18	M	94631	LE		2	c	2014	15
86	babu	48	M	62611	RE		2	c	2014	15
87	lakshmiamma	61	F	73846	RE		2	c	2014	15
88	asalammma	12	F	17826	LE		2	c	2014	15
89	muthuallu	61	M	37821	RE		2	a	2014	15
90	ganga	18	M	83479	LE		2	c	2014	15
91	delip	19	M	21455	RE		2	c	2015	15
92	ramasamy	39	M	818160	LE		2	a	2014	15
93	sankar	8	M	23571	RE		2	a	2014	15
94	kanniappan	34	M	220549	BE	A	2	e	2014	15
95	thanapa	38	M	82658	RE		2	c	2015	15
96	veraragavan	41	M	71309	LE		2	a	2014	15
97	thondan	16	M	301671	LE		2	c	2015	15
98	santhi	43	F	87124	RE		2	c	2014	15
99	pakiammal	12	F	26811	LE		3	a	2015	15
100	govindhammal	34	M	17863	LE		2	a	2014	15
101	arumugam	46	M	82504	RE		2	b	2015	15
102	chellamuthu	14	M	42781	RE		2	a	2014	15
103	kalaimugan	46	M	11137	LE		2	b	2015	15
104	mereaj	17	M	1550100	LE		2	b	2015	15
105	muthu	16	M	1550099	RE		2	a	2014	15
106	raghavan	23	M	242541	RE	D	2	e	2015	18
107	krishnan	32	M	1550147	LE		2	b	2015	15
108	masthan	29	M	1550131	LE		2	b	2014	15
109	kanniappan	13	M	1550189	RE		2	a	2015	15
110	chokalingam	42	M	1550107	LE		2	b	2014	15
111	ragavan	29	M	1550158	RE		2	b	2015	15
112	ramasamy	8	M	1550106	LE		2	a	2015	15
113	harini	20	F	1550137	LE		2	b	2014	15
114	elumalai	32	M	1550097	RE		2	b	2015	15
115	ramamurthy	15	M	1550102	LE		2	a	2014	15
116	lakshmanan	29	F	646347	RE		2	b	2014	15
117	gopal	38	M	789645	LE		1	b	2015	15
118	mariammal	56	F	91561	RE	G	3	e	2014	16
119	naveen	16	M	576547	LE		3	a	2015	17
120	saravanan	36	M	464674	RE		2	b	2014	15
121	kerena	20	F	123646	LE		2	b	2014	15
122	nalina	19	F	583528	RE		2	a	2014	15
123	chinnapayan	38	M	621868	LE		2	b	2015	15

1	2	3	4	5	6	7	8	9	10	11
124	andrews	13	M	548218	RE		2	d	2014	15
125	muthu	32	M	432716	RE		3	a	2015	15
126	rajesh	19	M	432175	LE		3	a	2014	15
127	nilla	32	F	334556	LE		2	a	2014	15
128	janani	19	F	572351	RE		3	a	2014	15
129	chandrasekar	19	M	324896	LE		2	b	2015	17
130	seetha	28	F	185723	RE		2	a	2014	15
131	kavin	11	M	537857	LE		2	b	2014	15
132	rahul	18	M	427158	RE		2	a	2015	15
133	prakash	65	M	531853	LE		2	b	2014	15
134	sridhar	21	M	916872	LE		2	a	2014	15
135	ramesh	43	M	981476	RE		3	b	2014	15
136	suresh	67	M	463853	RE		3	a	2015	15
137	revathy	15	F	471256	RE		3	b	2015	15
138	vaishnavi	11	F	231856	LE		3	a	2014	15
139	mythili	17	F	845725	LE		3	a	2014	15
140	sanmeli	24	M	471243	RE		3	a	2015	15
141	pooja	65	F	412653	RE		3	a	2014	15
142	arasu	42	M	934575	LE		3	b	2014	15
143	varun	18	M	132657	LE		3	a	2015	17
144	nithya	23	F	461537	RE		3	b	2014	15
145	balaj	12	M	471235	RE		3	a	2014	15
146	saravanan	30	M	23689	RE	B	2	a	2015	15
147	suganya	20	F	845757	RE		3	b	2015	15
148	murugan	46	M	462154	LE		3	a	2015	15
149	narayanan	15	M	734578	RE		1	a	2014	15
150	kodhandan	43	M	234567	RE		3	b	2015	15
151	raman	12	M	461537	RE		3	a	2014	15
152	meenakshi	27	F	987125	RE		1	d	2014	15
153	krishnan	7	M	123765	RE		3	a	2015	17
154	geetha	62	F	345678	RE		1	b	2014	15
155	maari	9	M	213567	RE		3	a	2014	15
156	sankar	47	M	987354	RE		3	d	2015	17
157	mahesh	22	M	345678	RE		1	d	2014	15
158	balaji	3	M	367908	RE		3	d	2014	15
159	panchashar	63	M	220820	LE	C	2	e	2015	18
160	chinni	51	M	123678	RE		1	d	2015	15
161	papamma	14	F	237890	RE		3	d	2014	17
162	venu	67	M	963170	LE		3	d	2015	15
163	raju	65	M	324567	RE		1	d	2015	17
164	murali	18	M	235612	RE		3	e	2015	15

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165	aravind	17	M	220820	RE		3	e	2014	17
166	unaamalai	14	M	356789	RE		3	e	2015	15
167	rani	45	F	301671	RE		3	e	2014	15